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PHONOSURGERY: INDICATIONS AND PITFALLS

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Twenty-five patients underwent type 1 thyroplasty (external medialization of abducted true vocal cord) during a 2-year period (1986 to 1988) at the University of Iowa. The most common indication for thyroplasty was post-thyroidectomy vocal cord paralysis. Eighteen patients (72%) had either a good or an excellent initial result. Five patients were revised. Postrevision, 21 patients (84%) had achieved either a good or an excellent result. Complications were limited to one case of significant vocal cord edema and another instance of vocal cord hemorrhage. No patient required a tracheotomy. No prosthesis extruded. We feel that phonosurgery has the advantages over traditional Teflon injection of allowing the patient's head to be in a neutral position during the operation; of allowing local anesthesia; of permitting a predictable, graduated end point of the procedure; and of being infinitely adjustable, with preservation of the vocal cord mucosal wave.

KEY WORDS — larynx, phonosurgery, thyroplasty, vocal cord paralysis.

INTRODUCTION

For nearly 20 years, Teflon injection has been the procedure of choice for correction of the unilaterally paralyzed vocal cord. Recently, however, a new procedure called phonosurgery (laryngoplasty, thyroplasty) has been developed and popularized that may offer distinct advantages over traditional Teflon injection in the correction of unilateral vocal cord paralysis and other cordal abnormalities. It is the purpose of this paper to review the experience at the University of Iowa with our first 25 patients undergoing type 1 thyroplasty (external medialization of abducted true vocal cord) and to report our results.

The procedure of Teflon injection is not without important limitations. The patient must be cooperative while under local or topical anesthesia for direct laryngoscopy. Difficulty with exposure of the larynx at the time of direct laryngoscopy may limit the success of the procedure. The patient's neck is in an abnormal position in the suspension laryngoscope, and he or she may be sedated and/or in distress during the procedure, both conditions that may make it difficult to determine the end point of injection and make for a poor result. The extreme hyperextension of the neck required for placement of a suspension laryngoscope also is not consistent with the position of the patient's neck and larynx during normal phonation. There is a need for certainty that motor function will not return to the injected vocal cord. In addition, Teflon is not recommended for the correction of vocal cord bowing. Finally, deficient soft tissue or extensive scarring of the cord limits the success of Teflon injection.

The position that Teflon takes in the soft tissue of the larynx into which it is injected is not highly predictable. It may migrate immediately downward to bulge the subglottic area, or medially to thicken the free edge of the cord. When it does, further injection is futile, because additional material will migrate to the same place. Once injected, the Teflon cannot be removed easily without significant damage to the vocal cord and may result in airway obstruction. The Teflon paste is engulfed by macrophages and becomes a hard granuloma within the tissues of the cord. This makes the cord stiff and nonvibratory, resulting in poor vocal quality. This granuloma may ulcerate the mucosa and become infected, proliferate, and require repeated debridement and produce an even worse voice. Once injected, Teflon's position and quantity are difficult to revise or reverse should the postoperative result not be acceptable.

Isshiki et al[1-4] began publishing their work on the modification of the voice by alteration of the external framework of the larynx in 1974. This work was extended to humans and was popularized in the United States by Koufman.[5] Modification of the voice by alteration of the external laryngeal framework is not new, and had been examined previously by Meurman,[6] Waltner,[7] and Sawashima et al.[8] Their work had been largely lost, however, in the enthusiasm for Teflon injection.

Phonosurgery has been demonstrated to be superior to the technique of Teflon injection in many ways.

1. The patient's head is in a neutral, relaxed position during the procedure, allowing a more accurate assessment of the vocal results.
2. It can be done readily with local anesthesia and sedation, allowing patient cooperation in voicing.

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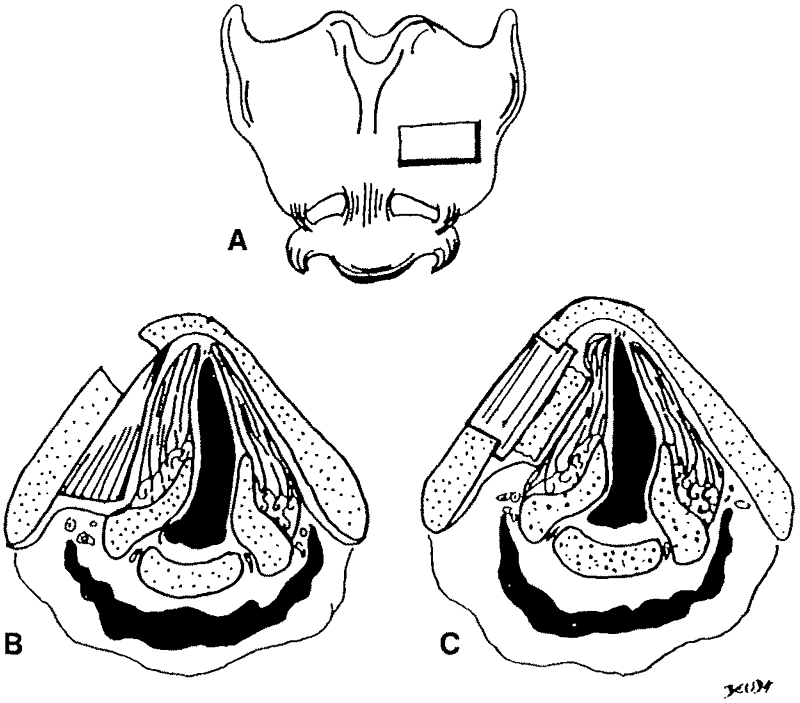
REPRINTS — Michael D. Maves, MD, Dept of Otolaryngology–Head and Neck Surgery, St Louis University Medical Center, 3635 Vista Ave at Grand Blvd, PO Box 15250, St Louis, MO 63110-0250.



Use of cartilage window in thyroid ala to allow medialization of true vocal cord. A) Position of window (inferior). B,C) Cross-sectional views at level of true vocal cord illustrating B) use of Silastic wedge to medialize vocal cord in patients with wide posterior glottic gap and C) use of T-shaped piece of Silastic to hold cord and portion of thyroid ala in medial position.

3. The final result is more predictable by both vocal and auditory end points.
4. The procedure is infinitely adjustable. One can adjust incrementally the Silastic shims used to hold the cord in a medialized position, in terms of both the amount of medialization and where the medialization takes place.
5. The technique has been employed successfully in patients with mobile but deficient cords with good results and without impairment of cordal mobility.
6. It is reversible, whereas Teflon injection is virtually not so.
7. Teflon granuloma is never an end result.

PREOPERATIVE ASSESSMENT

Preoperatively, the patient is examined jointly by the laryngologist and speech pathologist. In addition to the routine examination of the head and neck, preoperative videostroboscopy is performed on each patient. This study of vocal cord dynamics has become an indispensable part of the examination of each individual with any voice disorder. It is readily performed and allows careful inspection and analysis of the movement of the vocal cords by all members of the voice disorders team. The members of the team examine the videotape together and come to an agreement on, for example, how much of the voice disorder is functional and how much is mechanical, leading to the most appropriate treatment program.

SURGICAL TECHNIQUE

The operative procedure of type 1 thyroplasty is performed with local anesthesia. A flexible nasopharyngoscope is inserted that allows continuous monitoring of the larynx during the operation. The speech pathologist manages the video imaging during the operation. The image of the vocal cords is clearly visible to all members of the operative team during the manipulation of the larynx.

Initial exposure of the larynx is accomplished through a small transverse skin incision at the middle level of the thyroid ala. Blunt dissection between the strap muscles allows ready exposure of the thyroid ala on the involved side. A small window of cartilage will be outlined over the inferior portion of the ala (see Figure). Transillumination of the larynx with the light from the nasopharyngoscope usually identifies the position of the vocal folds. The incision in the cartilage window is begun with a knife. In older individuals, heavier instruments such as an oscillating saw or a rotating bur may be required to complete the cuts because of calcification. Once the window of cartilage is open, subperichondrial elevation of the lower endolarynx is carried out. The soft tissues of the endolarynx then are shifted medially and observed on the video monitor to find the position of the base of the true cord. The base then is shifted medially and held in position while vocalization indicates the best medial position and in which thirds of the cord this occurs. The gap created then is filled with a tailored Silastic wedge or wedges.

To provide effective medialization of the true cord, the window must be positioned inferiorly on the thyroid cartilage to be at the level of the true cord. The lower boundary of the window is 3 mm from and parallels the edge of the thyroid cartilage. The anterior limit of the window is 5 to 10 mm from midline. The window dimensions are altered individually, but in general are smaller for women and

TABLE 1. CAUSES OF VOCAL CORD PARALYSIS

Thyroid surgery	6
Chest malignancy	4
Vascular surgery	3
Neurologic	3
Postintubation	2
Senile bowing	2
Glomus vagale	2
Idiopathic	2
Laryngeal fracture	1
Congenital	1
Total	26

larger for men and average 5 x 10 mm. The posterior limit of the window should not approach the ascending portion of the cricoid cartilage.

Alternatively, a self-locking T-shaped piece of Silastic to hold the cord and an attached piece of thyroid alar cartilage in the determined optimal medial position are inserted through the window.

The wound is closed in layers with a Penrose drain. The patient is admitted overnight for observation of any evidence of hemorrhage, edema, or airway obstruction and is released the next morning. A short (5-day) course of antibiotics is administered, and the patient is placed on soft voice rest for 2 weeks.

MATERIALS AND METHODS

Twenty-six patients undergoing phonosurgery for medialization of an abducted vocal cord at the University of Iowa Hospitals and Clinics over 2 years form the basis of this study.

The videostroboscopic tapes for these patients were reviewed, and the results of the surgical procedure were compared to the preoperative recording. All patients demonstrated significant preoperative dysphonia or aphonia, aspiration, and inadequate cough due to abducted position of the vocal cord.

Postoperative results were classified as 1) no improvement; 2) improved (better) but still with residual symptoms of dysphonia, aspiration, or inadequate cough; 3) good; and 4) excellent. While there is some obvious overlapping in this grading system, we felt it captured the results of this initial group of patients and gave us some basis for comparison with other series.

RESULTS

The 26 patients consisted of equal numbers of men and women. The mean age of patients at the time of the phonosurgical procedure was 59.5 years. The cause of the vocal cord paralysis was varied (Table 1). The most common indication for thyroplasty was post-thyroidectomy vocal cord paralysis, and the second most common was paralysis resulting from mediastinal malignancy. Two patients had undergone previous treatment with Teflon paste, and two patients had been test treated with Gelfoam injection.

TABLE 2. RESULTS

	Initial Procedure	*After Revision*
No improvement	4	1
Improved	3	3
Good	9	11
Excellent	9	10
Total	25	25

Eight patients were treated with a wedge of Silastic placed between the inner perichondrium and cartilage of the thyroid ala to achieve medialization of the vocal cord. This procedure was selected for patients with a wide posterior glottic gap. Seventeen patients were treated with a T-shaped piece of Silastic to medialize the vocal cord and an attached piece of thyroid ala. This procedure was selected for cases of abduction or bowing of the vocal cord. In one case the procedure was aborted because manipulation of the laryngeal framework caused temporary airway obstruction. In one additional case, the lateral type 1 thyroplasty was combined with an anterior cordal tensing procedure to achieve an optimal result.

The initial results of the thyroplasty are given in Table 2. Eighteen patients (72%) had either a good or an excellent initial result. Three patients were felt to be improved, but their results were not optimal because of persistent hoarseness, occasional aspiration, or a poor cough. Four patients were felt not to have been helped by the procedure. Three of these patients have been revised, with good results in two and an excellent result in one. Two patients with improved but not optimal results also have undergone revision procedures, without further improvement, however. Postrevision, 21 patients (84%) have achieved either a good or an excellent result.

It should be emphasized that patients in the good and excellent categories demonstrated regaining of the mucosal wave motions on stroboscopy of the vocal cord when it was placed in apposition to the normal cord. This is distinctly different from our experience with patients we have studied post-Teflon injection, in whom we have seen that this coordinated wave motion of the affected cord was seldom achieved. Complications are detailed in Table 3. Our experience in this regard has been good. No patient required a tracheotomy, extruded the prosthesis, or experienced a wound infection.

TABLE 3. COMPLICATIONS

Intraoperative	
Vocal cord hemorrhage	1
Procedure aborted	1
Cordal edema	1
Perioperative	
Transient stridor (edema)	3
Postoperative	0

With the exception of the single patient in whom the procedure was aborted because of airway compromise with external manipulation, intraoperative complications have been limited to one case of significant vocal cord edema that interfered with the determination of the position of the abducted cord, and another instance in which vocal cord hemorrhage occurred because of tissue manipulation.

Perioperatively, three patients experienced transient respiratory stridor the same day of surgery that was due to edema of the larynx. None required a tracheotomy. The stridor was treated successfully with steroids and racemic epinephrine.

Postoperatively, five patients had a persistent glottic gap. While not all of these patients were dissatisfied with the result of the procedure, and indeed in some cases the results satisfied the patient, we felt that the gaps were undercorrected and that better results could have been achieved with a larger prosthesis.

DISCUSSION

Our series has confirmed the relative safety and efficacy of phonosurgery as a method of correcting the abnormally abducted vocal cord. We feel that although the technique is in evolution, it has such significant advantages over the traditional use of Teflon for medialization of the paralyzed vocal cord that we virtually have abandoned injections.

During our initial cases, we have discovered some technical points that we believe advance the state of the art. We have employed constant video monitoring of the manipulation of the vocal cord upon elevation of the internal perichondrium, which is very helpful in finding the cephalocaudal base of the true cord and then finding the visually optimal medialization. The final position of the vocal cord is determined by the sound of the patient's voice. Prolonged manipulation of the vocal cord sometimes causes edema of the cord, which may make this end point difficult to determine by the sound of the patient's voice alone, and the image of the edematous cord on the video monitor will allow the surgeon to take this swelling into account. We believe it is very important to limit the dissection to the subperiosteal space in order to minimize endolaryngeal edema and hemorrhage.

Additionally, this edema at the time of surgery may make the immediate results difficult to interpret. For that reason, we customarily have prefabricated several prostheses before entry into the laryngeal framework is made in order to limit the time of manipulation required. While each patient must have an individual, customized prosthesis because of individual variation, having several sizes of "T"s and wedges available allows the surgeon to modify the prosthesis rapidly before swelling of the cord makes fine adjustments difficult.

Our most successful phonosurgical results have been in previously untreated cases of isolated paralysis of the recurrent laryngeal nerve. Individuals who have been referred for treatment after prior Teflon injection have been treated less successfully by this technique. One of the reasons for this difference has been the destruction of the mucosal wave of the affected cord following injection of Teflon, which is not correctable by phonosurgery. In addition, the reverse bowing and fibrosis that may accompany Teflon injection may limit the amount of medialization that can be achieved by phonosurgery.

In review of the videostroboscope tapes, we have determined that our patients have been undercorrected more often than overcorrected. The reasons for this are several. One cause, which has been alluded to above, is that the cord becomes edematous with manipulation, and undercorrection may result once this edema subsides. Another reason may relate to fibrosis and scar tissue contraction around the implant following healing. Finally, there is the possibility of resorption of the thyroid cartilage abutting the Silastic prosthesis over time.

Some laryngologists have described the use of autologous cartilage for the prosthesis. We have continued to use Silastic because of its malleability, pliability, and ready availability, and also its reversibility as compared to Teflon. A comparative study to determine the best long-term material is desirable.

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LARYNGOTRACHEAL RECONSTRUCTION WITH COMPOSITE NASAL SEPTAL CARTILAGE GRAFTS

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The composite nasal septal graft has been used successfully by us to reconstruct patients with high tracheal and laryngotracheal stenosis. We have treated ten patients and have been able to decannulate seven of these patients. When these ten cases are added to the six original cases presented in an earlier report (1981), certain conclusions can be drawn. The success or failure of these procedures, which is judged by the ability to decannulate the patient, appears to be related to the extent of the initial injury. We discuss the indications for the composite nasal septal graft and the use of additional treatment, including stents, steroid injections, dilatations, and flaps. In conclusion, the addition of these ten cases to the original six cases of composite nasal septal grafts now provides the opportunity to review indications and contraindications for the use of this graft in the management of advanced laryngotracheal stenosis.

KEY WORDS — composite nasal septal cartilage graft, laryngotracheal reconstruction, laryngotracheal stenosis.

Reconstruction of the stenotic larynx and trachea still remains a challenge to the otolaryngologist. In the 1970s, renewed interest in treatment of advanced stenotic lesions of the upper airway led to the use of autogenous grafts interposed anteriorly in the airway. These grafts produced an improvement in the size of the airway lumen, usually resulting in decannulation.

The concept of using an autogenous graft interposed anteriorly in the airway was based on the work of Rethi[1] in the 1930s. Rethi proposed splitting the stenotic airway anteriorly and posteriorly and placing a stent to enlarge the airway. He felt that the scar tissue in the larynx should remain untouched in splitting the airway. The concepts that Rethi proposed are still true today. He can be considered the father of modern-day laryngotracheal reconstruction. Today, the most commonly used autogenous materials for airway augmentation are cartilage and bone from various anatomic sites.

Six cases of severe laryngotracheal stenosis reconstructed with the composite nasal septal cartilage graft were described in a preliminary report in 1981.[2] Ten additional cases of airway stenosis have been reconstructed since that time. The purpose of this presentation is to summarize and review this total of 16 cases.

MATERIALS AND METHODS

A retrospective review was conducted of all patients who have undergone reconstruction of the larynx or trachea with composite nasal septal cartilage grafts at the Vanderbilt University Medical Center and the Medical College of Wisconsin Affiliated Hospitals over the past 10 years. The cases were reviewed from the standpoint of age, sex, etiology, location of the stenosis, previous treatment, supplemental treatment, ultimate result, and follow-up. Success of therapy was judged by tolerance of decannulation.

The technique of graft procurement and placement has been described previously.[2] The graft is removed from the nasal septum by routine septoplasty techniques. The nasal septal cartilage with the attached unilateral respiratory mucoperichondrium is removed in composite, with preservation of the opposite mucoperichondrium (see Figure, A). A dermal graft is used to repair the nasal septal defect. The stenotic site is incised vertically. When the stenosis is subglottic or upper tracheal, the larynx and cricoid are split vertically in the midline. Also, the cricoid is split vertically, posteriorly (see Figure, B). Only when the stenosis is limited to the trachea can the trachea be split vertically without opening the cricoid or larynx.

The harvested composite nasal septal cartilage graft is trimmed to an elliptic shape. Care is taken to orient the composite graft to allow for ciliary flow from inferior to superior. The graft is wedged in a widened vertical midline airway incision at the site of stenosis, or placed in the hemilaryngectomy defect. The suturing of the graft is done in a manner that passes the suture submucosally through the cartilage both on the composite graft and the trachea and larynx (see Figure, C). The composite graft usually will take on a slight curvature as lateral re-

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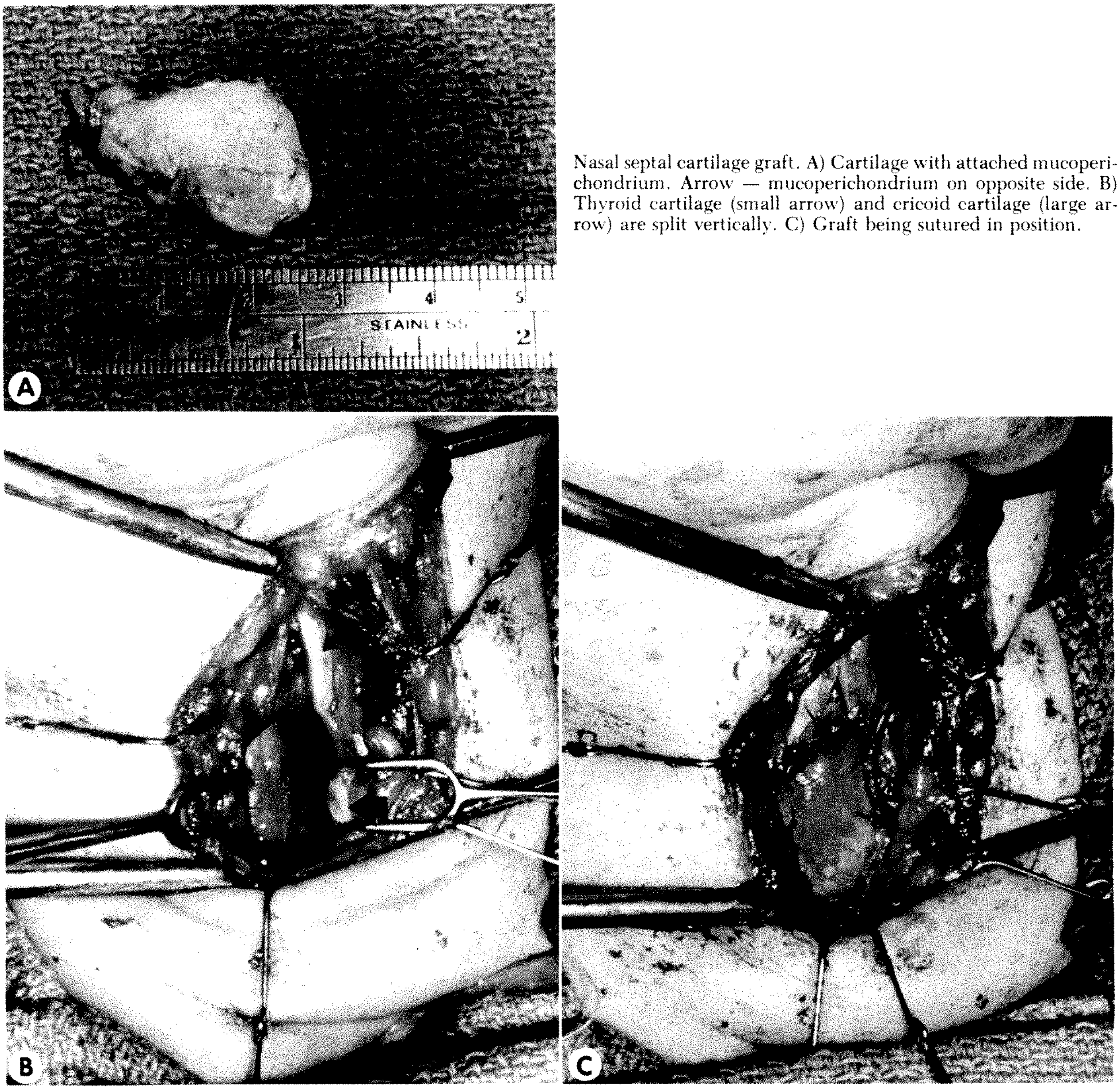

Nasal septal cartilage graft. A) Cartilage with attached mucoperichondrium. Arrow — mucoperichondrium on opposite side. B) Thyroid cartilage (small arrow) and cricoid cartilage (large arrow) are split vertically. C) Graft being sutured in position.

traction on the laryngeal and tracheal segments is released.

RESULTS

Sixteen patients with lesions of the larynx and/or trachea were reconstructed with composite nasal septal cartilage grafts (see Table). There were ten men and six women with an age range of 19 to 66. The need for reconstruction was caused by scar stenosis in 14 cases and laryngeal cancer in two cases.

The cause of stenosis was blunt trauma in seven cases, intubation injury in an additional six cases, and thermal injury plus intubation in one case. All 14 scar stenosis patients required tracheotomy because of their airway obstruction. Treatments prior to reconstruction are listed in the Table. These consist of dilatation, steroid injections, stents, arytenoidectomies, partial laryngectomies, dermal grafts, CO_2 laser excisions, and tracheal resections. Two patients had isolated tracheal stenosis, three patients had purely subglottic lesions, four patients had a glottic and subglottic stenosis, and five patients had combined glottic and upper tracheal stenosis at the time that reconstruction was performed.

Eleven of the 16 patients reconstructed have been decannulated and remain so with a follow-up of 6 months to 10 years. Voice quality is adequate in all of these patients, but most have a chronic hoarseness of varying degree. The period from reconstruction to decannulation extends from immediate to 10 months. Patient 6 delayed decannulation because of psychologic dependence on the tracheotomy, which had been present for 3 years. Patient 8 required arytenoidectomy to correct glottic stenosis prior to successful decannulation. Patient 10 had a 7-month delay because of persistent granulation that was

RECONSTRUCTION OF LARYNX AND TRACHEA

Patient No.	Age (yr)	Sex	Cause	Previous Treatment	Location of Persistent Stenosis	Interval to Reconstruction	Decannulation
1	55	M	Nasotracheal intubation, tracheotomy	Tracheotomy twice, Montgomery T-Tube stent, bilateral arytenoidectomy, right submucous cordectomy, dermal graft with stent	Tracheotomy site	26 mo	Immediate
2	58	M	Pneumonia, intubation	Tracheotomy twice, tracheal resection of 3.5 cm, repeated dilatations, repeated tracheal resection with complete mobilization, left arytenoidectomy, partial right laryngectomy	Subglottic, upper tracheal	22 mo	Not decannulated
3	65	F	Blunt trauma	Endoscopy, Silastic stent, repeated dilatations with steroid injections	Glottic, subglottic	22 mo	4 mo
4	19	M	Blunt trauma	Open reduction with stent, left cordectomy with stent, repeated dilatations with steroid injections	Glottic, subglottic	18 mo	1 wk
5	20	M	Blunt trauma, laryngotracheal disruption, bilateral vocal cord paralysis	Resection of first two tracheal rings and end-to-end anastomosis	Glottic, upper tracheal	7 mo	Not decannulated
6	23	M	Blunt trauma	Tracheotomy three times, right arytenoidectomy, repeated dilatations with steroid injections, excision of scar with dermal graft and stent, two scar excisions with carbon dioxide laser	Subglottic, upper tracheal	33 mo	6 mo
7	55	M	Prolonged cricothyrotomy	Tracheotomy, dilatations	Subglottic	18 mo	Postoperative respiratory arrest and death, no autopsy
8	22	M	Blunt trauma	Tracheotomy	Glottic, subglottic	18 mo	6 mo
9	60	F	Blunt trauma	Tracheotomy, open repair of laryngeal fracture	Subglottic	6 mo	Immediate
10	66	F	Intubation	Tracheotomy, laser arytenoidectomy	Subglottic, upper tracheal	4 mo	7 mo
11	42	F	Intubation, high tracheotomy	Arytenoidectomy	Posterior commissure, subglottic, upper tracheal	8 mo	4 mo
12	31	F	Intubation	Tracheotomy	Subglottic	6 mo	3 mo
13	36	F	Blunt trauma	Tracheotomy	Glottic, subglottic	12 mo	10 mo
14	40	M	Thermal injury, tracheotomy	Multiple dilatations	Tracheal	16 mo	Not decannulated because of persistent stenosis, decannulated after successful tracheal resection
15	42	M	Laryngeal cancer	Tracheotomy, hemilaryngectomy	N/A	Immediate	1 mo
16	42	M	Laryngeal cancer	Tracheotomy, hemilaryngectomy	N/A	Immediate	Edema for 6 mo with finding of recurrent cancer, treatment with total laryngectomy

relieved eventually by placement of a stent for 2 months. Patient 12 had recurrent granulations removed on four occasions over a 10-month period with subsequent successful decannulation.

The patients not decannulated deserve special mention. Only one of these is considered to have had a failure of the reconstruction. Patient 14 had a tracheal stenosis that failed placement of a composite nasal septal graft. The patient had a successful tracheal resection with end-to-end anastomosis. Patient 2 had an improved airway following reconstruction, but generalized tracheomalacia prevented decannulation. Patient 5 had an excellent subglottic and tracheal airway after grafting, but refused further therapy for the bilateral vocal cord paralysis that resulted from his original traumatic injury. Patient 7 died of a respiratory arrest on the second postoperative day. An autopsy was refused, and the exact circumstances of death are unknown.

The two cases of glottic cancer were T2N0M0 lesions. Reconstruction was performed immediately after hemilaryngectomy. Patient 15 was decannulated 1 month postoperatively and remains free of disease at 18 months. Patient 16 was an irradiation failure with persistent disease diagnosed 2 months following completion of external beam radiation therapy. Edema of the glottic region persisted following reconstruction of the hemilaryngectomy defect with a composite nasal septal graft. Six months after reconstruction, recurrent cancer was diagnosed and a laryngectomy was performed. The composite nasal septal graft was histologically viable despite previous irradiation and recurrent cancer, and the patient remains free of disease 14 months following laryngectomy.

DISCUSSION

The 10 years of experience with laryngotracheal reconstruction using the composite nasal septal cartilage graft provides certain insights as to indications. All patients were adults with advanced stenotic lesions, most having failed other treatment modalities. Children and teenagers with laryngotracheal stenosis are not repaired with composite nasal septal cartilage grafts.[3] The removal of nasal septal cartilage from the nose in children can cause injury to the nasal complex.

The stenotic site is important in selecting patients for airway reconstruction. All the stenosis patients except patients 1 and 14 had glottic, subglottic, or upper tracheal stenosis. The ability to gauge the stenosis is difficult even with tomograms. The most reliable indicator of airway compromise is the patient's ability to breathe through the compromised area. In addition, endoscopic examination with use of a general anesthetic is necessary. The stenosis then is sized by passage of a rigid bronchoscope through the obstruction. The obstructed area also is palpated with the tip of the bronchoscope to assess cartilage rigidity. Last, the tomograms of the airway are examined and correlated with the history and the results of the endoscopic examination. From reviewing our cases, it can be seen that all but two patients had high airway obstruction. To correct high obstruction usually requires some form of augmentation rather than a resection and reanastomosis.

The composite nasal septal cartilage graft provides excellent preservation and support of the airway. The previous histologic examination of composite nasal septal cartilage grafts revealed preservation of respiratory epithelium and transition to stratified squamous epithelium at the glottic level.[4]

Resorption of the nasal septal cartilage does occur with replacement by fibrotic scar tissue. This fibrotic scar tissue is dense and appears to provide suitable rigidity to the airway. Resorption of cartilage is variable. Some laboratory animals have had cartilage preservation when examined at 2 years.[5] This report also documents for the first time cartilage preservation in a previously reconstructed laryngectomy patient (patient 16).

The costal cartilage graft has been reported recently to be superior to the composite nasal septal cartilage graft.[6] However, it must be noted that basic laboratory research examining viability and amount of resorption is lacking. It is suspected that costal cartilage will be partially or completely resorbed, much as other cartilage grafts are. The resorption of cartilage appears to be a slow process, with the gradual replacement of cartilage by fibrotic tissue resulting in continued integrity of the airway.

With the increased awareness of the causes of stenosis of the laryngotracheal airway, it is felt that there will be fewer cases requiring reconstruction. The early management of the patient with a high risk of developing a stenosis can prevent further airway compromise.[7,8] The use of intralesional steroids for chronic stenosis in combination with dilatation also may be helpful in reducing the number of patients requiring reconstruction.[9] While carbon dioxide laser vaporization of scar often fails,[10,11] micro-trapdoor flap techniques with overlying mucosal preservation are proving to be successful in noncircumferential stenosis of the larynx and upper trachea.[12-14]

In conclusion, the composite nasal septal cartilage graft can be used successfully in patients with stenosis of the larynx and upper trachea. Stenoses up to 3 cm in vertical height can be augmented by the composite nasal septal graft. The respiratory epithelium on the composite nasal septal cartilage graft provides immediate resurfacing with a match of epithelium to the stenotic area. Although five patients in this report were not decannulated, only patient 14 is considered a failure of this technique. Reconstruction of moderate-sized defects of the larynx and upper trachea with composite nasal septal cartilage grafts is an excellent choice for adult patients.

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THE INTERNATIONAL SYMPOSIUM ON CLINICAL AND BASIC OTOLOGY

The International Symposium on Clinical and Basic Otology will be held June 4-6, 1990, in Beijing, People's Republic of China. The abstract deadline is December 31, 1989. For further information, contact the Beijing Institute of Otorhinolaryngology, Chan Liu, MD, Professor and Director, 17 Hougou Lane, Beijing 1000005, People's Republic of China.

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BEDSIDE VIDEOLARYNGOSCOPIC ASSESSMENT OF INTUBATION TRAUMA

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Telescopic laryngoscopic examination was performed at the bedside after extubation in 29 consecutive surgical intensive care unit patients who required endotracheal intubation for more than 16 hours. The examinations were documented with a portable video recording system. The majority of patients exhibited evidence of acute endolaryngeal trauma. Vocal fold ulceration and vocal fold motion abnormalities were the most common lesions. Patients with abnormal larynges were followed up after discharge from the intensive care unit. Most of the identified injuries resolved without intervention. However, silent aspiration was identified frequently in patients with vocal fold paresis and was thought to be a significant factor in postoperative pulmonary complications. Early identification of significant laryngeal trauma and/or vocal fold paresis in critically ill patients is important for both postoperative pulmonary care and voice rehabilitation. This pilot study demonstrated that documentation of the laryngeal examination is feasible in critically ill patients in an intensive care unit setting.

KEY WORDS — intubation trauma, larynx, videolaryngoscopy.

INTRODUCTION

The purpose of this study was to examine the changes seen in normal larynges after prolonged periods of endotracheal intubation. It has been our clinical observation that postintubation aspiration in the critical care patient can be a devastating complication for patients who already have compromised pulmonary function. This pilot study assessed the feasibility of routine documented bedside examination of the larynx in an intensive care unit setting.

METHODS

Twenty-nine consecutive patients in the surgical and pulmonary intensive care units were examined after extubation when they had required endotracheal intubation for a period of greater than 16 hours. A summary of patient data is provided in the Table. The patients averaged 62 years of age and had been intubated for 17 hours to 11 days. Nineteen patients were postoperative (15 open heart surgical and four general surgical patients) and had been intubated by an anesthesiologist under controlled situations. Ten medical patients were all intubated by house officers in the face of an acute or impending respiratory arrest. None of the patients had a history of laryngeal or voice abnormalities. Ten of the open heart surgery patients had normal findings on video-documented laryngeal examination prior to intubation. All patients received antibiotics for at least 1 week after extubation. Patients who had demonstrated laryngeal disease were reexamined every 4 weeks.

A 90° Hopkins rod indirect laryngoscope (Karl Storz 8702d) and a Medical Concepts Incorporated miniature color video camera were used for the bedside examinations. Light was supplied via a xenon light source (Karl Storz 487c) transmitted through a fluid-filled cable. Room air was pumped through the laryngoscope sheath to control fogging. For patients with low oxygen saturation, compressed oxygen was shunted through the airflow line during the examination.

The endoscopic image was monitored on a 9-in portable video screen that was placed on the head of the patient's bed. The image was recorded on ¾-in videotape. The videocassette recorder, light source, air pump, and monitor were carried to the bedside on a portable cart (Fig 1). Subsequent stop-frame analysis was done on a Sony U-matic VO-5800 videocassette recorder. Still photographs also were obtained by three methods. The clearest images were captured by attaching a single lens reflex (SLR) camera directly to the indirect laryngoscope. This method was used to document anatomic lesions such as vocal process granulomas. Images from the video record were made by taking photographs of the image on a video monitor with an SLR camera (Fig 2A), or by processing single video images with a freeze frame video recorder manufactured by Polaroid (Fig 2B). The latter method provided reasonably clear and instantaneous photographs that could be placed in the patient's chart.

RESULTS

After extubation, 28 of 29 patients (96%) complained of hoarseness. In each of these patients

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SUMMARY OF PATIENTS STUDIED

Pt	*Age (yr)*	*Length of Intubation*	*Reason*	*Time From Extubation to Initial Examination*	*Disorders*
1	77	17 h	CABG, AVR	5 h*	U, L, R
2	64	26 h	CABG	11 h*	LE, A
3	76	40 h	CABG, AVR	22 h*	U, G, L
4	63	93 h	CVA, RA	20 h	U, A, R
5	67	50 h	CABG	20 h*	U, L, A
6	74	49 h	AVR	24 h*	LE, R
7	66	11 d	RA	10 h	U, A, C, G
8	63	54 h	COPD, RA	20 h	U, A
9	40	13 h	WPW	22 h*	LE, R
10	74	21 h	CABG	11 h	U, P
11	70	6 d, 37 h	Laparo	18 h†	U, L, G
12	61	17 h	Sz, RA	5 h	U, L, C
13	62	65 h	Thorac	9 h	U, L
14	68	64 h	RA	20 h	U, L, A
15	70	20 h	CABG	20 h*	U, L
16	62	24 h	CABG	5 h	U, L
17	70	26 h	COPD, RA	4 h	U, P
18	60	24 h	Laparo	9 h	U, G, L
19	73	31 h	Laparo	20 h	U, L, A
20	60	24 h	CABG	10 h*	U, L
21	69	11 d	RA	3 h	U, L, A
22	64	96 h	CABG	20 h*	U, L
23	63	35 h	CABG	2 h	U, L
24	64	28 h	Laparo	8 h	U, L, A
25	66	48 h	CABG	24 h*	Normal
26	32	9 d, 45 h	Linton	2 h	P, A
27	60	28 h	CABG	2 h	U
28	59	27 h	RA	3 h	U, L
29	76	51 h	CABG	8 h	L

CABG — coronary artery bypass grafting, AVR — aortic valve replacement, RA — respiratory arrest, COPD — chronic obstructive pulmonary disease, WPW — atrial mapping for arrhythmias, Laparo — laparotomy, Sz — seizure disorder, Thorac — thoracotomy, Linton — Linton tube inserted, U — ulcers, L — lag of motion relative to opposite fold, R — arytenoiditis, LE — limited examination where videodocumentation was required for diagnosis, A — aspiration, G — granulomas, C — glottic chink, P — paralyzed cord.

*Preoperative examination was done.

†Examination was after second extubation.

there was demonstrable laryngeal trauma on documented examination. Three patients were aphonic. Twenty-two of the patients (76%) also had mild to severe odynophagia. All of the patients with these symptoms demonstrated visible laryngeal disease, and in each case the symptoms of hoarseness or dysphagia resolved prior to the resolution of the visible disease. Twenty-three patients had obvious ulcerations over the vocal processes of the arytenoid cartilages. Granulomas developed in five of these patients at the site of arytenoid ulceration (Fig 3). All of the granulomas healed without sequelae.

Vocal fold paresis was identified in 17 of the patients (59%). On follow-up, all but one of the pareses resolved. Motion abnormalities of the fold varied from obvious paramedian immobility of one or both true vocal folds to more subtle lagging of motion relative to the opposite vocal fold. Slow motion analysis of the documented examination facilitated identification of motion asymmetry. In cases of mild paresis, one fold appeared slightly shorter than the other and was delayed in adduction (Fig 2). In three cases, both folds were paretic. Stroboscopic analysis of patients recovering from unilateral vocal fold hypomobility showed flaccidity of the paretic fold with accentuation of mucosal waves during phonation. On follow-up examinations, the stroboscopic appearance remained distinctly abnormal in some of these patients, in contrast to normal results on standard examination.

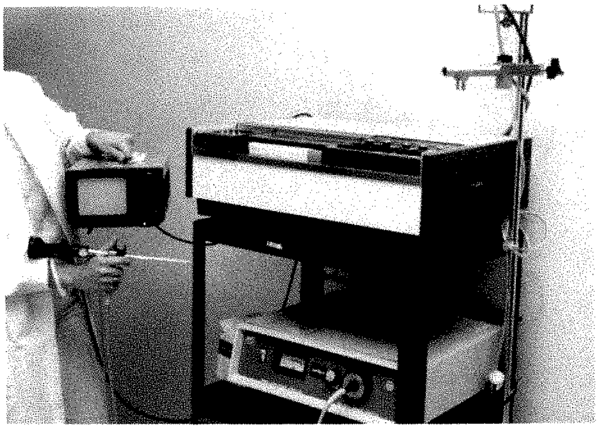

Fig 1. Portable videolaryngoscopic system. Can be moved to patient's intensive care unit bed on cart. Small monitor facilitates examination in critically ill patients.

Aspiration of secretions was documented laryngoscopically in ten of the 29 patients. Mild to severe aspiration was symptomatic for only three of these ten patients. Of the patients with documented aspiration on laryngoscopy, five developed frank aspiration pneumonia, and three of these patients subsequently died. Of the 19 patients who showed no evidence of aspiration on postextubation laryngeal examination, one developed pulmonary complications. Although aspiration was not observed during examinations, that patient did have significant laryngeal dysfunction with bilateral vocal fold hypomobility.

DISCUSSION

The risk of laryngeal trauma in association with prolonged endotracheal intubation has been well described and documented. In addition to immediate complications such as vocal fold hematomas, lacerations,[1,2] and arytenoid subluxation, prolonged intubation causes pressure-related damage to the larynx. Vocal fold ulcers, granulomas, and laryngeal motion abnormalities are thought to be related to pressure on the laryngeal tissues. Laryngeal damage has been reported to occur in approximately 6.2% of all intubated patients. Damage is more likely with increasing duration of intubation.[3]

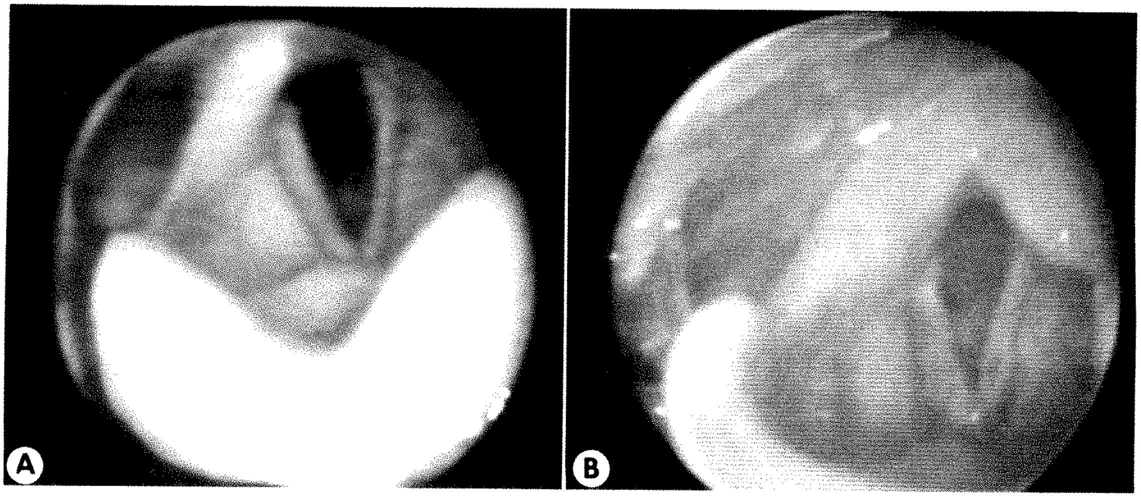

Fig 2. Photographs demonstrating documentation from single frame of video-recorded examination. A) Taken directly from video monitor screen with single lens reflex camera. B) Reproduced by use of Polaroid imaging device. Image can be placed immediately in patient's record. Patient's right vocal fold, seen on left in both reproductions, was delayed in its range and speed of movement. In this patient, who initially demonstrated aspiration, there was also asymmetry in distance from anterior commissure to vocal processes.

Mucosal ulcerations of the endolarynx probably occur with nearly every long-term intubation.[4] Although all areas that are in contact with the endotracheal tube may exhibit damage, the incidence is greatest for the glottic region. Burns et al[5] found that damage to the vocal apparatus occurred in most cases after 48 hours of intubation and that severe damage was seen with intubations of 72 hours or longer. Richter,[6] using an animal model, demonstrated respiratory cell degeneration after 2 hours of intubation, epithelial loss after 4 hours, and a well-defined ulcer after 36 hours. Donnelly[7] demonstrated in an autopsy study that in patients who had been intubated for 4 to 24 hours bacterial invasion was frequently seen in ischemic necrosis ulcers of the laryngeal epithelium. Because these epithelial ulcerations are bathed in bacteria-laden secretions, granulation tissue and perichondritis are frequent sequelae of exposure of the vocal processes of the arytenoid cartilage.[5] Cicatricial scar contracture affecting the airway may be a late sequela when there is bilateral loss of epithelium.[8]

Mucosal ulceration with granuloma formation occurs relatively infrequently in routine operative intubations of short duration, but may be seen in approximately 38% of prolonged intubation cases.[9,10] Ulcerations classically occur on the vocal process of the arytenoid cartilage and usually clear in 2 weeks to 2 months. Roughly 10% of patients who develop vocal process granulomas require endoscopic removal of these lesions, and there is a high rate of recurrence.[11]

Vocal fold paresis after intubation is a well-recognized complication,[12] and several reports implicate intubation as the cause of paresis,[13,14] even when the intubation is without trauma.[15] Most frequently, studies have described an immobile fold in the paramedian position, with a return of normal function within 2 months.[16] Bilateral paralysis has been observed and may result in acute airway obstruction[17] and aphonia.[14] A spectrum of laryngeal neuromuscular dysfunction may be associated with intubation damage[18]; however, it appears that permanent paralysis is infrequent.

Although a toxic neuritis from anesthetic agents or from chemicals used to make the tube has been suggested to be a factor in some cases,[14] laryngeal neuromuscular dysfunction is most likely due to endolaryngeal compression of the recurrent nerve.[19] Cavo,[12] in a series of ten cadaver dissections, demonstrated that the anterior branch of the recurrent nerve is vulnerable to compression between an expanded endotracheal tube cuff and the overlying

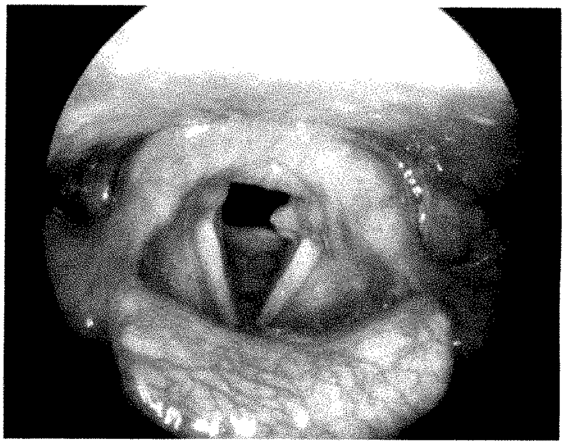

Fig 3. Photograph taken with single lens reflex camera attached to Berci-Ward 90° laryngoscope (Karl Storz). Granuloma over left vocal process is demonstrated. This method provides superior documentation, but requires two examinations and some delay in processing of film, with possibility that satisfactory picture is not obtained.

thyroid cartilage. The intermediate fold position often observed after intubation-related paresis may be explained by selective injury to the anterior branch of the recurrent laryngeal nerve.

Several factors have been associated with the development of laryngeal damage after prolonged intubation. These include the size of the tube in relation to the size of the larynx[20]; the shape and chemical composition of the tube and cuff[14]; the inflation pressure of the cuff; movement of the tube as it passes through the glottis; the placement of the tube; and the medical condition of the patient.[21,22] A tube that is too large or poorly curved will cause more pressure on the underlying arytenoid or cricoid mucosa.[22,23] Excessive head movement, swallowing, or neck extension in the restless patient will aggravate these pressure effects.[14]

Cuff pressure is thought to be a major factor in laryngotracheal damage. There is a direct correlation between the degree of airway damage and the severity of respiratory failure, mainly because a need for high peak end-expiratory pressure levels requires higher cuff pressures.[10] Diabetic patients, immunocompromised patients, and patients with infected secretions also have an increased incidence of complications from intubation.[21]

As critically ill patients survive for longer periods of time using ventilators, the incidence of laryngeal damage will be expected to increase. Reported studies have used several methods to identify laryngeal damage, including speech analysis,[24] mirror examinations,[1] and endoscopic examination.[10,25] Transnasal fiberoptic endoscopy permits unhurried examinations of the glottic apparatus,[26] but lacks the clarity of rigid techniques.[27] Rigid telescopic videolaryngoscopy provides superior documentation of anatomic and pathologic changes of the larynx and allows close inspection of vocal fold function.[28,29]

Bedside videolaryngoscopy proved to be an easy, reliable method of examining the larynx in these critically ill patients. These examinations were well tolerated and without incident. Slow motion analyses of examinations that were more difficult often revealed disorders that may not have been appreciated by the naked eye.

Visual images of the larynx were reproduced for documentation in the patients' records by three methods. Photographs taken through the laryngeal telescope via an SLR camera provided superior resolution (Fig 3), but required a delay for film processing. In addition, it was more difficult to be certain that the examiner had captured a frame that appropriately demonstrated the disorder. Single frame images from the video record were obtained by direct photography from a video monitor, or by immediate reproduction with a Polaroid video image reproduction device (Fig 2). The latter method provided less clear resolution, but had the advantage of immediate documentation for the patient's medical record. This method also had the advantage of more effective communication of the findings to the patients' attending physicians. The video reproduction methods required less examination time and were more likely to capture a frame that demonstrated the disorder. The quality of this type of reproduction has continued to improve and to decrease in cost.

When ulcerations were identified, the patients were followed closely to detect the earliest phases of granuloma formation. Bacterial invasion of mucosal ulcers has been shown to occur early and may lead to progressive laryngeal damage.[30] Contaminated tracheal secretions are reported to complicate laryngotracheal injury; hence, antibiotic therapy should be administered at the earliest sign that serious mucosal injury has occurred from intubation.[31] Serial examinations will identify patients who are developing significant posterior commissure scar tissue. There is some evidence that early endoscopic dilatation and division of such scar tissue may result in a better outcome.[24]

This study demonstrated that significant laryngeal damage may occur with intubation as early as 17 hours. These early laryngeal injuries, particularly when associated with aspiration, may be more critical to the short-term survival of the patient than the development of chronic sequelae that are less common. We feel that for patients who have required endotracheal intubation for more than 12 hours, direct laryngoscopy should be performed after extubation and prior to oral feeding to assess the possibility of significant, possibly life-threatening laryngeal injury. Minor pulmonary aspiration may be devastating for critically ill patients. Because even minor vocal fold paresis can be associated with silent aspiration, oral feedings should be delayed until the larynx is functioning normally.

CONCLUSIONS

1. Detailed bedside examination of the larynx is feasible in the critically ill patient in the intensive care unit setting.
2. Neuromuscular dysfunction of the glottis is common after intubation for longer than 16 hours. Although most cases resolve within a week, aspiration in the first few days after extubation may cause serious pulmonary compromise.
3. We recommend that all patients intubated for longer than 12 to 24 hours should have documented laryngoscopy performed after extubation.
4. Stroboscopy may be helpful for the identification of subtle vibratory abnormalities resulting from paresis or scarring.

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IMPLANTATION OF THE MELBOURNE/COCHLEAR MULTIPLE-ELECTRODE EXTRACOCHLEAR PROSTHESIS

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The Melbourne/Cochlear multiple-electrode extracochlear implant is designed for deaf patients who are unsuited to multiple-electrode intracochlear implantation. The implant consists of a receiver-stimulator package connected via a lead wire assembly to six individual stimulating electrodes. There is a choice of two alternative surgical procedures, both of which are via a combined middle ear approach using anterior and posterior tympanotomies. Four active electrodes shaped into compressible platinum-iridium soft-balls are fed through the mastoid cavity and across the facial recess, and placed into cavities that are made over the cochlear turns that project to the medial wall of the middle ear. One hard-ball active electrode is placed into the round window niche. One hard-ball reference electrode is placed into the hypotympanum. An additional electrode wrapped around the lead wire assembly can be used as an alternative reference electrode. A specially designed insertion needle facilitates the placement and the fixation of the soft-ball electrodes.

KEY WORDS — hearing loss, multiple-electrode extracochlear prosthesis.

INTRODUCTION

Multiple-electrode intracochlear implants have proved to be superior to single-electrode implants in many patients.[1] Not all patients, however, can benefit from a multiple-electrode intracochlear implant. Chronic otitis media, labyrinthitis ossificans, and possibly malformations of the inner ear can render the patient unsuited to an intracochlear device, and the possibility of residual hearing and the associated risks of otitis media can make intracochlear implantation unsuitable for infants and young children. Otitis media, however, has not been demonstrated to be a risk for extracochlear electrode placement.

Although studies have shown that some pitch discrimination can be obtained by extracochlear stimulation at different sites over the cochlea,[2] this finding is not conclusive. Nevertheless, multiple-electrode extracochlear stimulation may be preferable to single-electrode extracochlear stimulation not only because of the possibility of providing additional place pitch information, but because multiple electrodes provide a choice of stimulus electrodes that can reduce the inherent side effects of extracochlear stimulation, in particular stimulation of the facial nerve, the tympanic branch of the glossopharyngeal nerve, and the vestibular nerve.

In a preliminary anatomic study on six human temporal bones it was concluded that an extracochlear electrode array placed via a combined middle ear approach would overlie less than a third of the length of the cochlear turns.[3] This would limit the number of electrodes that could be used, and five active electrodes are recommended from this study. This recommendation was based on the anatomic findings and the assumption that the size of each electrode would not exceed 1 mm in diameter. This placement of the electrodes should be close enough to individual nerve fiber groups and provide channel separation.

This presentation describes two surgical approaches for the Melbourne/Cochlear multiple-electrode extracochlear implant. The preservation of the middle ear ossicles was considered important when developing the first approach. In the second, better access to the middle ear is achieved, but with limited loss of middle ear structures.

DESCRIPTION OF IMPLANT

The Melbourne/Cochlear multiple-electrode extracochlear implant is shown in Fig 1. The titanium package containing the stimulator electronics and the receiver coil are the same as those of the conventional intracochlear device and are placed underneath the skin. The section containing the titanium package has a diameter of 22 mm and is 6 mm thick. This section is placed into a circular bed drilled in the temporal bone. The section containing the receiver coil and a titanium-encapsulated magnet for attaching the transmitter coil is 24 mm wide

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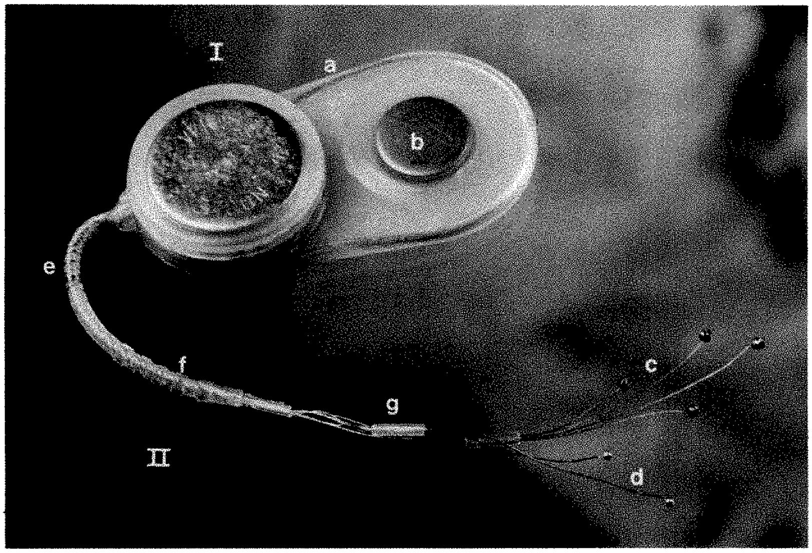

Fig 1. Photograph showing Melbourne/Cochlear multiple-electrode extracochlear implant device. I — receiver-stimulator package, II — electrode array, a — receiver coil, b — magnet, c — electrode soft-balls, d — electrode hard-balls, e — reference electrode, f — ripples, g — Silastic collar.

and 3 mm thick. The whole device is embedded in medical-grade Silastic. The lead wire assembly contains six Teflon-coated platinum (90%)-iridium (10%) wires with a diameter of 100 μm that are spiralled to protect against metal fatigue. These wires are embedded in a Silastic tube with an outside diameter of 2 mm. The lead wire assembly emerges from the receiver-stimulator device at an angle of 45° and is 35 mm long. The electrode array consists of six individual wires. Four active electrodes are held together with a movable Silastic collar. This facilitates their introduction through the posterior tympanotomy and placement over the cochlea. The group of four active electrodes terminates distally in platinum-iridium soft-balls. These balls are made by loosely winding the terminal 40 mm of the platinum-iridium wires. The length of these active electrodes is staggered. The shortest is 35 mm and they increase in 5-mm steps to a length of 50 mm. This facilitates the placement of the electrodes at different locations. The two electrodes that terminate distally in a platinum-iridium hard-ball have a diameter of 1 mm. One of these electrodes can be selected as a reference electrode, and the other as an active electrode placed into the round window niche. The lead wire assembly is wrapped around proximally with bared platinum-iridium wire for a distance of 15 mm and acts as an alternative reference electrode. The thick part of the lead wire assembly is rippled for better fixation with the Dacron mesh ties.

SURGICAL PROCEDURES

Two alternative surgical approaches are described and may be chosen according to the surgeon's preference.

Procedure 1. An incision is made in the postaural sulcus through skin and subcutaneous tissue and extended superiorly and posteriorly to create an inferiorly based flap.[4] An anteriorly based deep fascial and periosteal flap also is created. A partial cortical mastoidectomy is performed, and the short process of the incus and the lateral semicircular canal are identified. A posterior tympanotomy is carried out after visualizing the course of the facial nerve, and the round window niche exposure is the same as for intracochlear implantation.

The skin of the osseous external ear canal is incised from a point superiorly, at the 12-o'clock position, through 270° around the anterior and inferior aspect of the canal to create a posterosuperiorly based tympanomeatal flap. The flap is pushed backward, and the fibrocartilaginous ring of the tympanic membrane is mobilized from the tympanic sulcus as far as is necessary to expose the round window niche. As the cochlea lies beneath the wall of the anterior part of the middle ear, it is not necessary to remove the malleus or other ossicles for access. Better access to the cochlea through the anterior part of the middle ear also may be achieved by exposing the anterior recess of the ear canal and by removing bone over the temporomandibular joint. A thin bony plate is left over the joint for protection. The package bed and the groove for the electrode lead wire then are created. This procedure is the same as that described for the Melbourne/Cochlear multiple-electrode intracochlear receiver-stimulator.[5]

After the package bed is prepared, the tensor tympani muscle is resected where it runs across the apical region of the cochlea. This is facilitated by opening its bony canal and slightly reducing the inferior ridge of the canal with use of a diamond bur. A 0.6-mm diamond bur is used next to drill the anteroinferior overhang of the round window niche to accommodate the active hard-ball electrode, and a groove for the electrode wire is drilled in the overhang superiorly (Fig 2). The positions are selected for the four active soft-ball electrodes to be placed directly over the cochlear turns that project to the

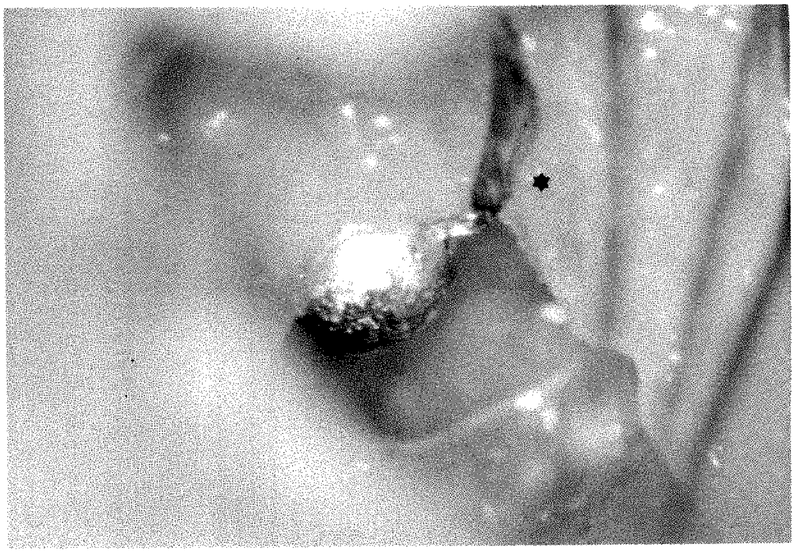

Fig 2. Photograph through external ear canal demonstrating groove (star) in posterosuperior overhang of round window niche and placement of hard-ball electrode.

medial wall of the middle ear. The sites for the cavities are chosen to ensure that all electrodes are separated by at least 1 mm. The electrode position over the apical region of the cochlea is drilled first (Fig 3). This electrode should lie toward the apex of the triangle bordered by the internal carotid artery, the eustachian tube, and the bony bed of the tensor tympani muscle. A 0.6-mm diamond bur is used to drill a saucer-shaped cavity in the bone without exposing the endosteum of the cochlea. Entry into the cochlea can be avoided if notice is taken of the appearance of the endochondral bone while drilling. When the bone changes from a woven texture to an amorphous ground-glass appearance, there is only a thin layer of bone remaining. The drilling should cease at this point and certainly before a blue line appears. The cavity is undermined to create an overhang. Two electrode positions over the middle turn are drilled on a direct line connecting the anterior edge of the oval window with the internal carotid artery (Fig 3). With a 1-mm diamond bur two cavities again are drilled into the bone until the appearance of the bone changes as described above. With a 0.6-mm bur the bone is undermined to create an overhang. A fourth electrode position is drilled over the basal turn on the promontory (Fig 3), and this cavity is made in the same way. The tympanic nerve is resected where it runs across the promontory. The resection of the nerve is necessary in order to drill a cavity in the promontory and to avoid pain on electric stimulation.

After cavities are drilled in the bone overlying the cochlea, the electrodes are put into position. One hard-ball or stimulating electrode is inserted first and fed into the middle ear via the aditus ad antrum. The electrode is passed anterior to the stapes and the wire is placed in the groove in the superior overhang, and the electrode ball in the round window niche (Fig 2). The second hard-ball or reference electrode is inserted into the middle ear via the posterior tympanotomy and placed into a hypotympanic cell. This electrode can be chosen as an alternative reference electrode to the one wrapped around the proximal lead wire. The soft-ball stimulating electrodes then are inserted into the middle ear via the posterior tympanotomy. This procedure is facilitated when the Silastic collar is pushed distally. After the insertion, the Silastic collar is moved backward to allow better handling of each individual electrode. The soft-ball electrode with the longest wire is placed apically and pressed into the prepared cavity with the angled blunt insertion needle (Fig 4). This then is followed by the second-longest electrode, which is placed into the prepared cavity overlying the proximal portion of the middle turn, and the third-longest electrode, placed into the cavity overlying the distal portion of the middle turn. The soft-ball electrode with the shortest wire is placed into the cavity in the promontory overlying the basal turn.

The receiver-stimulator is placed into the package bed and the electrode lead is fixed with Dacron

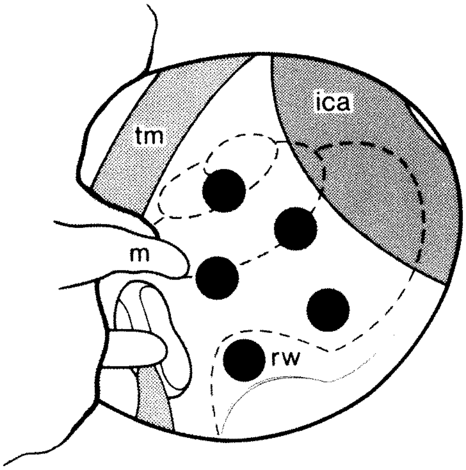

Fig 3. Diagram showing sites for electrodes. m — handle of malleus, tm — tensor tympani muscle, ica — internal carotid artery, rw — round window.

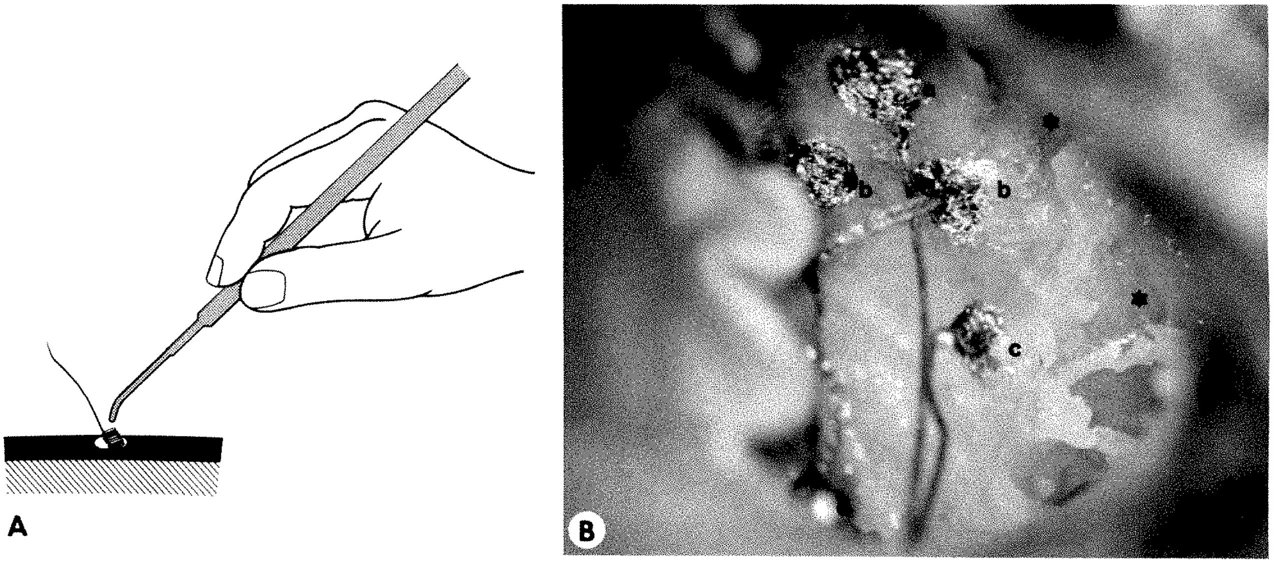

Fig 4. A) Diagram demonstrating insertion needle being used to fix soft-ball electrodes into cavity in bone overlying cochlea. B) Photograph through external ear canal demonstrating hard-ball and soft-ball stimulating electrodes in position. a — soft-ball electrode in apical region of cochlea, b — soft-ball electrodes over middle turn, c — soft-ball electrode on promontory, d — hard-ball electrode in round window niche, stars — internal carotid artery.

mesh ties. The wound is irrigated with an antibiotic solution. Fascia is placed over the electrodes for additional support. The tympanomeatal flap is repositioned, gauze packed into the ear canal, and the wound closed. Finally a pressure dressing is applied.

Procedure 2. Similar to the Heermann incision, the endaural incision begins in the floor of the ear canal close to its entrance and runs around the canal's posterior wall to the 12-o'clock position. It then extends superiorly in the incisura terminalis between the crus of the helix and the tragus before proceeding posteriorly around the upper part of the auricle in a wide curve, finishing about 80 mm behind the postaural sulcus (Fig 5). The skin, subcutaneous tissue, muscle, and periosteum are incised simultaneously to create an inferiorly based flap that includes the auricle. The limited mastoidectomy, package bed, groove for the electrode lead wire, posterior tympanotomy, and exposure of the round window niche are completed as described for procedure 1.

The posterior and superior osseous walls of the external ear canal are removed carefully, with the skin preserved. Alternatively, the posterior wall of the external ear canal could be thinned carefully and then cracked forward still attached to the canal skin to ensure its viability. Both the skin and the eardrum are pushed forward. To do this it is necessary to remove the incus and the head of the malleus, and cut the tendon of the tensor tympani. The middle ear is now wide open. The tensor tympani muscle then is resected, and the drilling of cavities and the fixation of electrode balls is completed according to the description for procedure 1. All electrodes are fed through the mastoid cavity and across the facial recess into the middle ear.

The outer ear canal is filled with Gelfoam to reform its original shape. The posterior and superior walls then are rebuilt with bone meal mixed with fibrin glue (available in the Federal Republic of Germany). The remaining surgical steps are completed as described for procedure 1.

DISCUSSION

Not every cochlear implant candidate is suited to a multiple-electrode intracochlear system. A very young age, labyrinthitis ossificans, and possibly

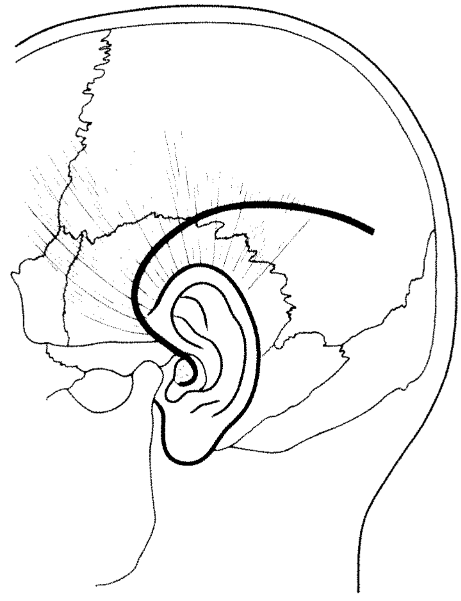

Fig 5. Diagram showing incision for alternative middle ear approach for multiple-electrode extracochlear implantation.

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malformations of the inner ear can render the deaf patient unsuited. In these cases an extracochlear device is an alternative.

Multiple-electrode intracochlear devices give better speech perception results than single-electrode intracochlear or single-electrode extracochlear devices.[1] These advantages are attributed to the closeness of electrodes to individual nerve fiber groups so that the tonotopic organization of the cochlea can be used. In order to achieve similar results with an extracochlear system it would be necessary to place an equal number of electrodes as close as possible to individual nerve fiber groups around the cochlear turns. Multiple-electrode extracochlear devices may be able to stimulate localized groups of auditory nerve fibers on a place basis, but for the results to be comparable to those for multiple-electrode intracochlear stimulation it would be important to maximize the number of electrodes that can provide discrete stimulation of auditory nerve fibers. This is likely to be difficult because of the distance of the electrode from the auditory nerve fibers and the small length of the cochlear turns underlying the medial wall of the middle ear.

The number of electrodes that can be placed over the cochlea is determined by the length of the cochlear turns that project to the medial wall of the middle ear, the size of the electrodes, and the surgical approach chosen. The total length of the cochlear turns ranges from 31 to 33 mm.[6] According to our own anatomic studies it appears that 9 to 10 mm of the cochlear length is accessible via an endaural middle ear approach.[3,7] This means that less than a third of the whole cochlear length would be available for the placement of electrodes. Our findings, however, are in contrast to those of anatomic studies that indicate that more than half of the cochlear turns are accessible via an endaural middle ear approach.[8-10]

Our anatomic studies show that the restricted access is caused by the internal carotid artery, the facial nerve, and the middle cranial fossa, and also by the temporomandibular joint, which limits access to the cochlear turns from a posterolateral direction, and not anterolaterally. Because the axis of the cochlea lies in an anterolateral and superior direction and because access to the cochlea is only possible posterolaterally, the turns of the cochlea that face the coronal plane anteriorly and the middle cranial fossa superiorly are not accessible.

The restriction that only 9 to 10 mm of the cochlear turns can be reached via an endaural middle ear approach without destroying major structures of the middle ear raises the question of the number of electrodes it is practicable to place over these turns. Since the size of each electrode is about 1 mm, and for good electric insulation and channel separation the distance between the electrodes should be at least 1 mm, a restricted number of only five electrodes appears to be possible. Despite this restriction, the selected cavities along the cochlear turns allow the placement of one electrode over the apical region, two electrodes over the middle turn, one electrode over the basal turn, and one electrode in the round window niche.

The electrode cavities are drilled with 0.6- and 1-mm diamond burs. It is important that the cavities are made deep enough for adequate current flow through the cochlea, but drilling must be stopped as soon as the texture of the bone changes and before a blue line becomes visible. When further drilling is carried out there is danger of breaking into the cochlea. The preservation of the endosteal lining is possible only when drilling is stopped before the blue line is reached. Studies have not yet demonstrated to what extent bone underneath the electrode impairs the localized stimulation of spiral ganglion cells.

The cavity over the apical turn is the most difficult one to make with procedure 1, because of the angle of approach to the anterior part of the cochlea. When a 1-mm bur is used, only a groove can be made in this area. A 0.6-mm bur, however, will enable a cavity to be drilled instead of a groove. This difficulty does not arise with procedure 2 because of a more favorable angle of approach to the medial wall of the middle ear. Additionally, the generous exposure of the medial wall of the middle ear in procedure 2 is safer for the horizontal portion of the seventh nerve. The improved exposure, however, is accomplished through the loss of the malleus head and the incus. The cavities over the middle and basal turns are much easier to drill, as access is good with both procedures.

The placement of the hard-ball stimulating electrode in the round window niche is carried out best via the aditus ad antrum prior to the placement of the soft-ball electrodes. A hard-ball electrode inserted into the middle ear via the posterior tympanotomy can sit insecurely, because small movements of the electrode wire are transmitted immediately to the tip, and displacement can occur. On the other hand, movements applied to the electrode array (inserted via the aditus ad antrum) are not so likely to be transmitted to the electrode tip in the round window niche (B.K.-H.G.F., G.M.C., D. M. Bloom, unpublished observations). Furthermore, inserting the hard-ball electrode after the soft-ball electrodes can be difficult because of obstruction from other wires.

The fixation of the soft-ball electrodes is accomplished best when an adequate bed is prepared. This is achieved by undermining the bone with a 0.6-mm diamond bur and thus creating an overhang. The soft-ball tip pressed into such a bed will sit firmly. Four electrodes placed in this manner can lift a temporal bone weighing about 100 g. The soft-balls are pressed into the holes with a blunt, angled needle (Fig 4A). Pressure must not be excessive, however, or a break into the cochlea will occur.

Two options are available for the reference electrode. One hard-ball electrode can be placed into a hypotympanic cell. This may allow current flow away from the facial nerve. The alternative reference electrode wrapped around the lead wire assembly would correspond to an electrode placed close to the temporal muscle.

Clinical experience has been obtained with three patients. The results will be published elsewhere. Preliminary evaluation 6 months after implantation showed that their performance was equivalent to group 3 of 75 Hannover patients who received multiple-electrode intracochlear implants.[11]

SUMMARY

The Melbourne/Cochlear multiple-electrode extracochlear receiver-stimulator has been described. Two surgical procedures for its implantation have been outlined. Procedure 1 provides access with the preservation of the ossicles. Procedure 2 provides better access for the placement of an electrode over the apical turn, but the malleus and the incus need to be removed. Five stimulating electrodes are placed over the cochlear turns that project to the medial wall of the middle ear. One soft-ball electrode is placed over the apical region of the cochlea, two soft-ball electrodes over the middle turn, one soft-ball electrode over the basal turn, and one hard-ball electrode in the round window niche. There is an option of two reference electrodes, one a hard-ball electrode placed into a hypotympanic cell, and the other an exposed wire around the proximal lead wire and near the temporal muscle.

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ENDOSCOPIC PROBLEMS DUE TO CERVICAL VERTEBRAL DISEASES

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The authors draw attention to cervical spine disorders that limit mobility of the vertebrae and thereby interfere with esophagoscopy. Four orthopedic disorders that either fuse the cervical spine or produce massive osteophytes are discussed and exemplified by specific cases, and appropriate techniques for endoscopy are recommended.

KEY WORDS — cervical spine, endoscopy, vertebral disease.

INTRODUCTION

This paper discusses selected cervical vertebral diseases that complicate or preclude esophageal endoscopy. A review of these disorders, the clinical examination, the radiographic evaluation, and the techniques of endoscopy are presented.

Diseases of the vertebral structures may limit the mobility of the cervical spine and interfere with an esophageal endoscopic examination. There are four pathologic processes that partially or completely fix the cervical vertebrae in an erect alignment or impinge upon the pharyngoesophageal lumen, obstructing insertion of the endoscope. These lesions include the Klippel-Feil syndrome, Forestier's disease, ankylosing spondylitis, and massive osteophytic overgrowth from cervical arthritis.

HISTORICAL REVIEW

The history of the evolution of endoscopic equipment, including the contemporary flexible fiberoptic era, is fascinating and should be enjoyed by all practicing endoscopists. References[1-7] are cited for the interested reader; however, a comprehensive review is beyond the scope of this paper.

The topics of position, anesthesia and sedation, instrumentation, the physical areas of endoscopy, and the anatomic factors impacting on the procedure will be considered insofar as they relate to the topic of vertebral disease.

The classical procedures taught by Chevalier Jackson are described and illustrated in several publications.[4,5] The position of elevation and extension of the head with proper flexibility of the cervical spine is shown in Fig 1A. The proper position for rigid endoscopy straightens the cervicoesophageal angle and facilitates the initial passage of the rigid scope into the cervical esophagus. Jackson emphasized the difficulty in examining the lower esophageal segment due to the anterior location at the level of the diaphragm; further extension of the head brings into line the gastroesophageal junction (Fig 1B).

Among the many other concepts that Jackson discussed[4,5] was the status of anesthesia for endoscopic examination. He strongly recommended local anesthesia and indicated a preference for cocaine supplemented by proper psychic preparedness. In retrospect, this prejudice reflects the perilous state of anesthesia in the early 20th century.

A second consideration emphasized by Jackson was the anatomic configuration of the patient's vertebrae and musculoskeletal flexion, and he cited several specific disorders of the spine that interfere with passage of the scope beyond the middle third of the esophagus.

Insertion of the flexible fiberoptic units, by contrast, may not be compromised by the anatomic features that preclude rigid intubation. Additionally, the cervicoesophageal angle is of less importance because of the flexibility of the instrument within the esophageal channel. Because the instrument can be inserted relatively easily, sedation and local anesthesia may be minimized. Finally, even the most difficult areas can be visualized with pneumatic inflation and retroflexion of the instrument.

CERVICAL-VERTEBRAL DISORDERS

KLIPPEL-FEIL SYNDROME

Klippel-Feil syndrome (congenital synostosis of the cervical vertebrae) was first described in 1912. This entity is a congenital disorder of unknown cause and is characterized by the triad of low posterior hairline, short neck, and limitation of motion due to a failure of segmentation of the cervical vertebrae.[8] The vertebral fusion may involve two segments or appear in the extreme form of a congenital blocked vertebra. Other associated, nonskeletal disorders include defects in the genito-

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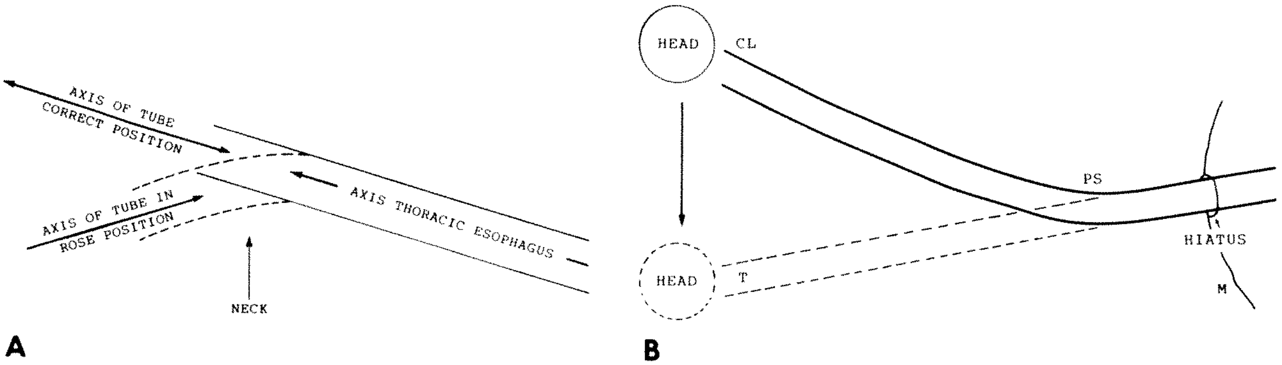

Fig 1. Modified from Jackson and Jackson.[5] A) Proper position and pharyngoesophageal axis for rigid endoscopic examination. B) Insertion of rigid esophagoscope into lower esophageal segment as facilitated by dropping head. CL — cervical level, PS — passing thoracic esophagus, T — depressed position of head, M — diaphragm.

urinary, nervous, and cardiopulmonary systems and deafness. The clinical appearance of the short-necked individual with prominent webbing should raise suspicion of the underlying vertebral disorder. Limitation of cervical motion is related to the number of fixed vertebrae; fewer than three or a fusion in the lower cervical area may not produce a detectable impairment of motion.

The diagnosis is established by a radiographic examination that depicts fusion of the cervical vertebrae, from a two-level synostosis to massive fusion.

Case 1. This 49-year-old man (Fig 2) underwent radiographic investigation for an obstruction in the region of the lower esophagus. The preliminary cervical view indicated a monoblock including the C-2 to C-7 vertebrae. The spot views and whole-column contrast films demonstrated a stricture at the lower esophageal segment; whether it was benign or malignant could not be established radiographically. An endoscopic examination confirmed a benign inflammatory stricture associated with reflux esophagitis.

FORESTIER'S DISEASE

Forestier's disease,[9] also classified as diffuse idiopathic skeletal hyperostosis, is a common disorder of middle-aged and elderly men (6:1 male to female ratio) that occurs in 6% to 12% of autopsy material.[10] The usual clinical features include aching and spinal stiffness with minimal evidence of spinal immobility. In the early stages of the disorder the stiffness is confined to the thoracolumbar spine, however, within several years approximately 40% of patients develop lumbar and cervical area symptoms. Five of 23 patients reported by Utsinger et al[10] complained of dysphagia; in three it was of sufficient severity to be the presenting symptom.

The pathologic condition includes ossification of the paraspinal connective tissue, the peripheral portion of the disc annulus, and the anterior spinal ligament.[9,10] The process appears to be progressive, with gradual fixation of the cervical spine.

Utsinger et al[10] described the radiographic evidence of diffuse idiopathic skeletal hyperostosis as distinctive and stated that the diagnosis could be established satisfactorily with the support of other, extraspinal manifestations. Forestier and Rotes-Querol[9] described the stages of progression by sequential radiographic studies that initially include prevertebral thickening, opacification, and spur formation, and finally complete bridging of the disc by a single spur that is later incorporated into the spurs from the adjacent vertebrae.

Other disorders included in the radiographic differential diagnosis are intervertebral osteochondrosis, spondylosis deformans, ankylosing spondylitis, and metabolic disorders such as hypoparathyroidism, chronic fluoride intoxication, and ochronosis.[11]

Case 2. This 73-year-old man presented with symptoms and radiographic evidence of an obstructing carcinoma of the lower third of the esophagus. On clinical examination the patient demonstrated a relatively immobile neck with virtually no flexion or extension. Indirect pharyngoscopy revealed a submucosal mass at the level of

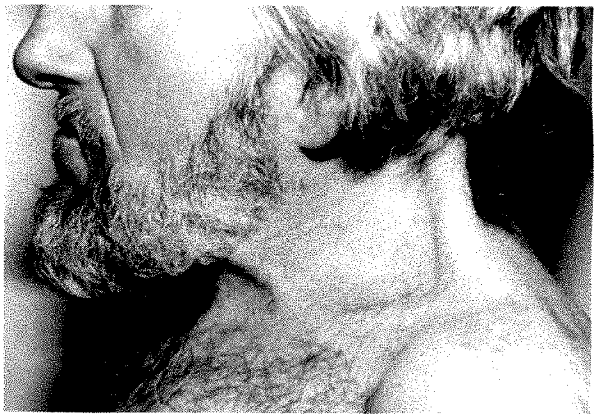

Fig 2. (Case 1) Klippel-Feil syndrome. Patient has short immobile neck, pterygium colli, and low hairline. (From Welsh LW, Welsh JJ, Chinnici JC. Combined techniques of esophagoscopy. Trans Am Broncho-Esophagol Assoc 1987:122-9. Reprinted with permission.)

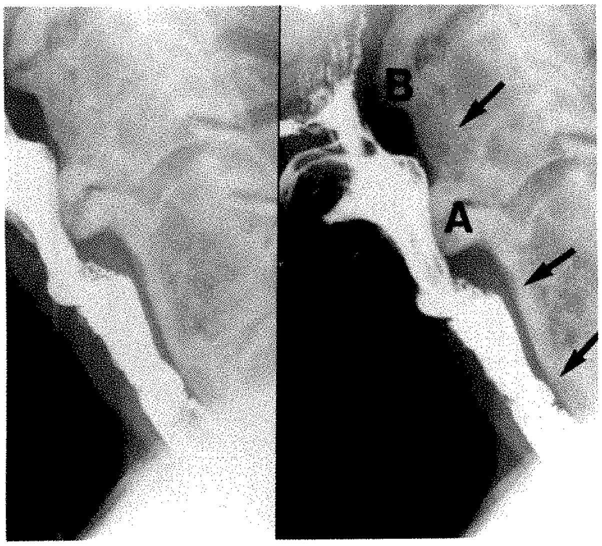

Fig 3. (Case 2) Forestier's disease. Arrows — thickening and ossification of anterior spinal ligament with cervical fixation; A, B — spurs bridging cervical vertebrae. (From Welsh LW, Welsh JJ, Chinnici JC. Combined techniques of esophagoscopy. Trans Am Broncho-Esophagol Assoc 1987:122-9. Reprinted with permission.)

the laryngeal inlet compatible with an osteophytic deformity of the cervical vertebrae. Lateral cervical vertebral films were taken in conjunction with the barium contrast study and identified osteophytes, thickening, and ossification of the anterior spinal ligaments, loss of disc space with fusion, and impingement upon the posterior pharyngeal wall (Fig 3). In spite of this radiographic evidence, the patient denied difficulty with initiating swallowing or the passage of a food bolus into the midesophagus. Flexible esophagoscopy and biopsy confirmed a malignant neoplasm of the distal esophagus.

ANKYLOSING SPONDYLITIS

Ankylosing spondylitis is a progressive, chronic, inflammatory disease occurring in 1% to 1.5% of the population, with a symptomatic onset in young adult life. It is approximately equal in incidence between the sexes. The etiologic factors are not fully known, but there is a genetic predisposition for susceptibility related to the HLA-B27 antigen.[11,12]

The pathologic process of ankylosis appears to be the final phase of reossification and bridging of the cartilage space following the earlier stages of chronic inflammatory reaction, osteitis, and localized osteoclastic destruction. Ossification of the lateral surfaces of contiguous discs produces a "bamboo spine." Similar activity on the vertebral body may occur at the anterior surface of the disc.[13]

The radiographic evaluation of ankylosing spondylitis is contingent upon the stage of the disease, namely, inflammation, bone destruction, and finally ossification. The appearance of the syndesmophytes bridging the intervertebral discs and progression to osseous fixation are the classic features of ankylosing spondylitis.

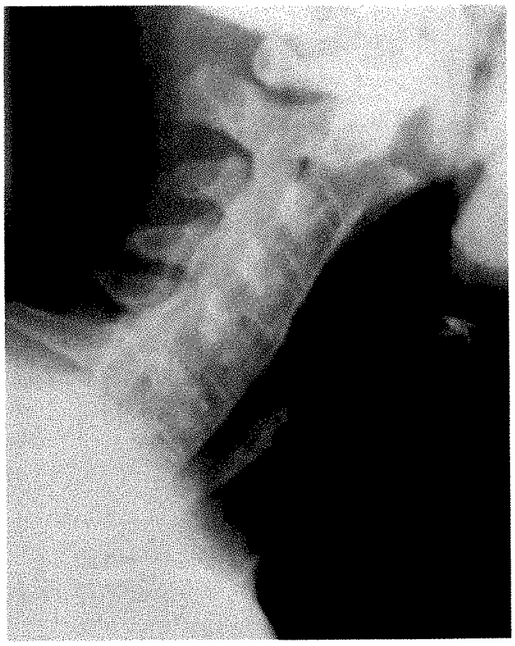

Fig 4. (Case 3) Ankylosing spondylitis. Bridging of anterior bodies by syndesmophytes and fixation into bamboo spine characterize advanced stage of disease.

Case 3. This 62-year-old woman suffered progressive fixation and limitation of the spine for many years and, more recently, partial esophageal obstruction as a result of strictures in the proximal and distal esophagus due to pemphigoid. Prior to endoscopic examination, a lateral film of the cervical vertebrae demonstrated ankylosing spondylitis (Fig 4). Preoperative awareness of the limiting anatomic factors permitted successful esophagoscopy.

DEGENERATIVE OSTEOPHYTES

Degenerative osteophytes of the cervical vertebrae may occur in the advanced state of degenerative joint disease or osteoarthritis. This condition usually is observed in the elderly patient and only infrequently produces symptoms. When it is symptomatic, however, anterior expansion of the osteophytes may produce dysphagia due to an obstructive mass on the posterior pharyngeal wall.[14-16] While ligamentous stress may contribute to the formation of spurs, the primary mechanism appears to be a degenerative change in the intervertebral fibrocartilaginous discs, secondarily from the vertebral bodies, and the posterior apophyseal articulations.

The radiographic examination displays osteophytes in various degrees of formation, arranged horizontally and often coalescing to fuse with several contiguous vertebrae. From a regional view the vertebrae below the fourth cervical level are more frequently involved than levels 1 to 3.

Case 4. This 68-year-old man complained over several years of progressive pharyngeal obstruction

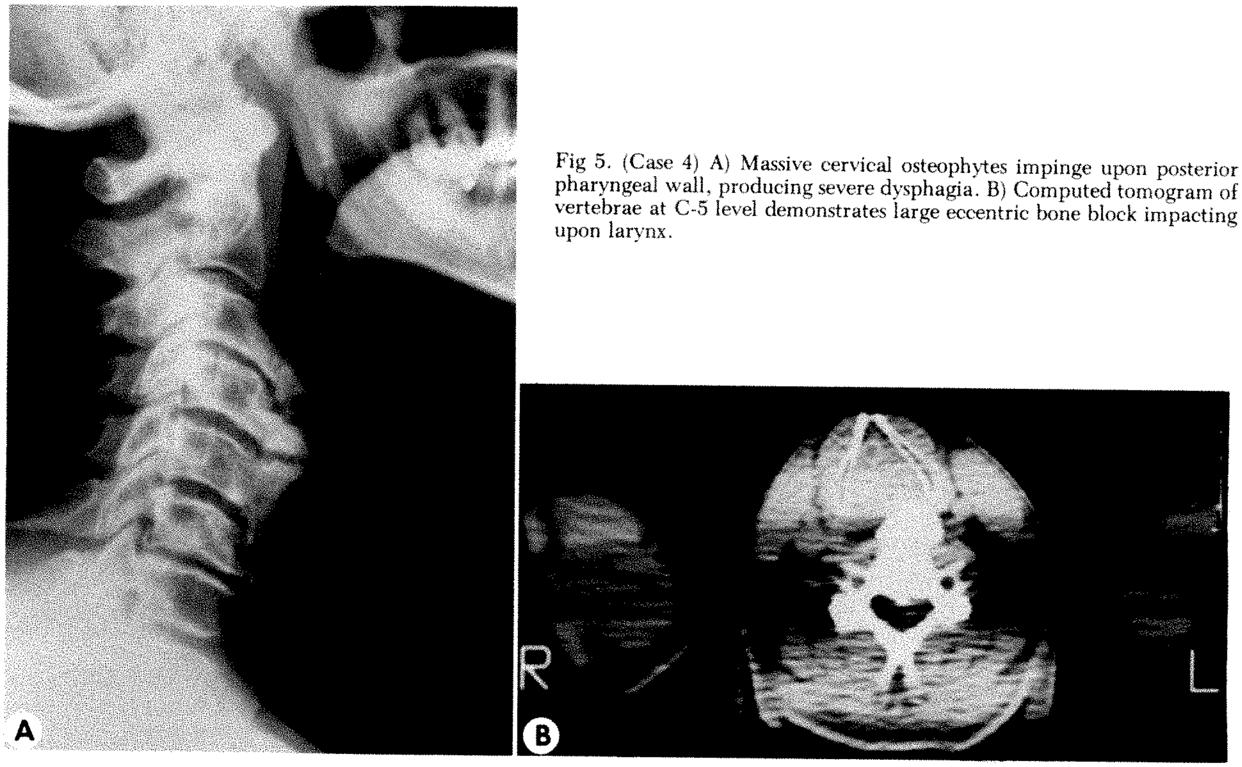

Fig 5. (Case 4) A) Massive cervical osteophytes impinge upon posterior pharyngeal wall, producing severe dysphagia. B) Computed tomogram of vertebrae at C-5 level demonstrates large eccentric bone block impacting upon larynx.

to solid foods. Generalized osteoarthritis was evident in his extremities and the thoracolumbar spine. Indirect laryngoscopy revealed a posterior pharyngeal mass impinging upon the epiglottis. Obtained as a preliminary to the esophagram, lateral cervical films illustrated the polly beak deformity beginning at C-3, further exaggerated spurs at C-4 and C-5, and minilipping at C-6 and C-7 (Fig 5A). A computed tomogram of the vertebrae demonstrated an eccentric new bony growth from the body of C-5 impacting upon the pharynx (Fig 5B). The barium column was modified by the osteophytes, and the left hypopharyngeal region was described as distorted by extrinsic compression. A combined endoscopic approach was employed to examine the pharynx and cervical esophagus, which identified only abnormalities related to the cervical osteophytes.

TECHNIQUE

The choice of the endoscopic instrument is contingent upon the following factors: 1) the purpose of endoscopy, eg, examination, biopsy, removal of foreign body per endoscopic dilatation; 2) the location of the lesion; 3) the configuration of the patient, ie, flexibility of the cervical and thoracic vertebrae; and 4) the anesthetic agent.

In each of these vertebral disorders flexibility of the cervical vertebrae is diminished markedly, and in case 4 the difficulty of intubation was compounded further by obstructive cervical osteophytes. It is immediately apparent that a rigid esophagoscope of the Jackson type cannot be employed because of an unfavorable cervicoesophageal angle. As an alternative, the narrow-diameter pediatric flexible panendoscope may be used successfully in these conditions.

During intubation with the flexible system, the individual with the Klippel-Feil deformity appears to have an obstruction at the level of the vocal cord with a functional narrowing at the hypopharyngeal inlet. The condition of skeletal hyperostosis that is further compounded by prominent anterior cervical osteophytes limits passage of the rigid scope because of impaction upon the submucosal bone ledges. Additionally, because of a fixed cervical angle, identification of the esophageal inlet is difficult. Ankylosing spondylitis can be associated with other problems such as limitation of the mandibular excursion and total immobility of the cervical vertebrae. While the flexible fiberoptic instrument usually is passed into the cervical esophagus without direct visual control, cervical osteophytes of the magnitude illustrated in case 4 preclude this technique. Further extension of the neck exaggerates the obstruction of the osteophytes, at which point the scope either impacts upon the bony wall or deflects anteriorly toward the larynx. In each of these disorders a combination of rigid and flexible instrumentation can be employed satisfactorily to visualize the cervical inlet and to achieve the endoscopic goal.

Since the procedure requires exceptional patient cooperation, we prefer general anesthesia. Because of the anatomic configuration the airway intubation is via the nasal route and may be an "awake intubation" with sedation and local anesthesia or a visually controlled fiberoptic nasal intubation. Subsequently a rigid laryngoscope or short cervical esophageal speculum may be inserted to elevate the larynx, widen the posterior hypopharynx, and intubate the esophagus with the forward-viewing flexible fiberoptic esophagoscope. The open-blade laryngoscope may be removed at this point, or the tubular esophagoscope may be retained in place until completion of the examination.

While we have described this technique for four cervical disorders, it is applicable to other entities limiting vertebral excursion, such as 1) fracture of the cervical vertebrae, 2) immobilization due to anterior or posterior cervical fusion and cervical injuries limited by the halo apparatus, 3) lesions with destructive or osteolytic components in the cervical vertebrae, such as osteomyelitis and metastatic carcinoma, and 4) demineralizing disorders of the bony structures, including severe osteoporosis and osteitis fragilitas.

In summary, cervical vertebral diseases may affect the technique of esophagoscopy, and the fixed or flexible instrument alone may not be satisfactory for the examination. In this event, a combination of techniques may be employed to achieve the endoscopic goal.

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RECURRENT ADULT ACUTE EPIGLOTTITIS: THE ROLE OF LINGUAL TONSILLECTOMY

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Acute epiglottitis is a life-threatening infection of the supraglottic airway that can occur at any age. Although it is traditionally described as a childhood infection, recent reports describe an increased recognition of this problem in adults. When appropriate and timely therapy is instituted, this condition is generally self-limited. Recurrent acute epiglottitis is exceedingly uncommon, and its treatment rarely is addressed. We encountered and treated a case of recurrent acute epiglottitis in an adult. After the third recurrence, careful consideration was given to possible pathophysiologic mechanisms and potential therapeutic options. Further recurrence was prevented effectively by performing a lingual tonsillectomy. Although this is an unusual condition, the cause of recurrent acute epiglottitis may be related to chronic lingual tonsillitis. Lingual tonsillectomy in these cases may help prevent further recurrent episodes.

KEY WORDS — epiglottitis, tonsillectomy.

INTRODUCTION

Acute epiglottitis, also referred to as supraglottitis, is a life-threatening infection of the supraglottic larynx and can cause rapid airway compromise. Although it is traditionally considered a childhood disease, persons of all ages can be affected. Since recurrent episodes are unusual, proper diagnostic and treatment options have not been well defined. The case of a woman who experienced three episodes of acute supraglottitis is presented. Possible pathophysiologic mechanisms and a guide to evaluation and management are discussed.

CASE REPORT

A 20-year-old woman presented after 36 hours of sore throat, dysphagia, odynophagia, a slight choking sensation, and mild airway compromise. Although her past medical history was remarkable for recurrent erythema nodosum, she had no other rheumatologic symptoms. Three years prior to admission an acute episode of supraglottitis had been treated by observation in an intensive care unit, high dose antibiotics, and steroids. No artificial airway had been required, and she recovered completely.

On physical examination she was quite anxious and was experiencing some dysphagia, but was tolerating her secretions adequately. The anterior part of her neck was tender but not edematous. Her oropharynx was slightly erythematous, but no exudates were noted. Although her faucial tonsils were surgically absent, her lingual tonsils were hypertrophic and inflamed. The entire supraglottic larynx was pale, markedly edematous, and visually obscuring the endolarynx.

She was treated with intravenous cefuroxime, steroids (dexamethasone), and observation in the intensive care unit. Blood cultures were not performed, but a pharyngeal culture yielded *Hemophilus influenzae* (non-β-lactamase-producing). The inflammation and edema decreased substantially after 48 hours of treatment, and she was discharged on a regimen of oral antibiotics after the fifth hospital day. Two weeks later examination revealed persistently hypertrophic lingual tonsils and a pale, omega-shaped, slightly edematous epiglottis.

One month later a third episode of supraglottitis prompted reevaluation. The epiglottis and arytenoids were slightly erythematous and edematous, and her lingual tonsils and adenoids were prominent and inflamed, but her airway appeared stable. Since she was very reliable and lived close to the hospital, outpatient treatment with amoxicillin with clavulanic acid and Solu-Medrol was instituted. After 8 hours of therapy, a subjective response to treatment was noted, and by 24 hours, obvious symptomatic improvement was accompanied by markedly diminished inflammatory changes. Laboratory tests performed included a complete blood count (CBC), ESR, urinalysis, C1 esterase inhibitor levels, serum immunoglobulin electrophoresis, antinuclear antibody, and rheumatoid factor. Findings from these studies were all unremarkable. Direct laryngoscopy with biopsy of the epiglottis was performed. A moderate, nonspecific, submucosal chronic inflammatory cell infiltrate was seen on histopathologic examination.

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Since epiglottic edema and lingual tonsil hypertrophy persisted despite a 45-day trial of inhalant steroid therapy, lingual tonsillectomy was performed. Histopathologic examination revealed marked lymphoid hyperplasia, but findings were otherwise unremarkable. She has experienced no further episodes of supraglottitis, despite two subsequent episodes of pharyngitis. Examination 18 months postoperatively revealed a small, omega-shaped epiglottis with a normal-appearing glottis, laryngeal inlet, and arytenoids.

DISCUSSION

Prior to 1940, epiglottitis was considered a childhood disease. With over 200 cases of adult epiglottitis reported, it has now emerged as a clinically important infection in adults. Recurrent epiglottitis is an unusual problem that has been addressed in only two previous reports.[1,2] Although Mustoe and Strome[3] described two patients who experienced five separate episodes in a series of 70 patients with epiglottitis, no specific discussion of recurrent epiglottitis was presented.

Because recurrent epiglottitis is such an unusual problem, a search for underlying pathologic conditions affecting the supraglottic larynx should be undertaken. Conditions causing chronic inflammation and edema of the supraglottic larynx include collagen vascular disorders, granulomatous diseases, angioedema, amyloidosis, myxedema, chronic fungal or mycobacterial infections, and lymphoma and other neoplasms. A complete clinical evaluation for these potential problems must be performed when recurrent epiglottitis is encountered.

The chronic supraglottic inflammation occasionally associated with collagen vascular disorders might result in recurrent acute episodes or chronic epiglottic edema.[4] A history of joint pains or dermatologic problems, a previous rheumatologic diagnosis, or a family history of rheumatologic problems might raise the suspicion of this diagnosis. A thorough joint evaluation and a complete dermatologic survey should be included in the general physical examination. The laboratory evaluation should include ESR, CBC, rheumatoid factor, antinuclear antibody, and complement levels. Rheumatologic consultation is extremely helpful for diagnosis and treatment of patients with suspected collagen vascular diseases.

Of the granulomatous diseases, sarcoidosis occasionally involves the supraglottic larynx.[5] A careful history of pulmonary symptoms, night sweats, or other constitutional symptoms might raise the possibility of sarcoidosis producing the recurrent supraglottic inflammation. A thorough physical examination should be performed, with emphasis on the pulmonary and peripheral lymphatic systems. Laboratory tests should include chest radiography and an angiotensin-I converting enzyme test. A tissue diagnosis ultimately might be necessary prior to beginning treatment.

Although angioedema and myxedema can both produce chronic or recurrent supraglottic edema, these conditions rarely produce symptoms of acute inflammation. While the medical history is often diagnostic in these cases, a laboratory evaluation for C1 esterase inhibitor level (angioedema) and thyroid function tests (myxedema) can confirm these suspicions.

The possibility of unusual infectious causes should be evaluated carefully. A thorough history should include questions regarding foreign travel, venereal diseases, chronic cough, and weight loss. A complete physical examination should be accompanied by an appropriate laboratory evaluation including CBC, chest radiography, fungal serologic tests, skin tests, and syphilis serologic tests. A biopsy of the involved tissue for culture and histopathologic examination is often crucial to confirming the diagnosis.

Lymphoma or other malignancy must also be considered. While a history of smoking or excessive alcohol use often raises the suspicion of malignancy, this diagnosis is even more likely when regional and distant adenopathy is noted. An endoscopic biopsy with histopathologic examination is always necessary prior to instituting therapy.

Another possible cause of recurrent supraglottitis is contiguous spread from chronically infected adjacent structures (specifically Waldeyer's ring). In the early 1900s supraglottitis was considered a secondary infection, a theory to which early authors such as Theisen (1900),[6] Thomson (1920),[7] and Brown (1940)[8] subscribed. Today, most authors consider it a primary infection of the supraglottic larynx. The similar lymphatic drainage patterns for both the lingual tonsils and the supraglottic larynx, as well as the absence of a significant anatomic "barrier" between these contiguous structures, support a theory based on contiguous spread of infection. Although our patient had undergone a faucial tonsillectomy as a child, the impressive size of her lingual tonsils during acute episodes and on follow-up examinations implicated them in the development of these recurrent episodes. These clinical findings also were noted in the case described by Blome and Small.[2] In their case epiglottectomy and lingual tonsillectomy successfully prevented further recurrence. The status of the lingual or faucial tonsils in the report by Swedo et al[1] was not described, and a specific surgical treatment was not addressed. We believe that lingual tonsillectomy in our case eliminated the focus of chronic infection responsible for these recurring episodes.[2] Resolution of the chronic epiglottic edema despite two subsequent episodes of acute pharyngitis further supports this clinical impression.

In conclusion, recurrent acute adult epiglottitis is a rare condition. The acute episodes should be treated with appropriate airway management, antibiotics, and steroids. A complete clinical evaluation should be performed to uncover local or systemic diseases accounting for this recurrent or chronic problem, and treatment in these cases must be directed at the underlying pathologic process. When secondary contiguous spread of infection from chronically inflamed regions of Waldeyer's ring is suspected, lingual tonsillectomy may play a role. By eradication of these adjacent regions of chronic infection, the potential morbidity associated with recurrent episodes of epiglottitis might be prevented.

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CALL FOR PAPERS
SECOND INTERNATIONAL COCHLEAR IMPLANT SYMPOSIUM

The University of Iowa Department of Otolaryngology–Head and Neck Surgery and the International Cochlear Implant Association will hold the Second International Cochlear Implant Symposium in Iowa City on June 4-9, 1990. The symposium will focus on basic science aspects of electrical stimulation on the auditory system, new cochlear implant strategies, clinical application in both adults and children, and rehabilitation and educational issues. Please submit abstracts to Bruce J. Gantz, MD, Department of Otolaryngology–Head and Neck Surgery, University of Iowa Hospitals and Clinics, Iowa City, IA 52242.

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AUDITORY BRAIN STEM RESPONSE MONITORING DURING MIDDLE EAR SURGERY

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Conductive hearing loss can be determined in the course of middle ear surgery by sound probe stimulation and simultaneous recording of auditory brain stem responses. Mechanical properties of the ossicular chain, usually judged subjectively by the surgeon's visual and tactile senses, can be quantified objectively. Thus, disarticulation of ossicles can be localized precisely, and fixation of the head of the malleus can be differentiated from stapes fixation. Moreover, the function of the reconstructed ossicular chain or prosthesis may be ascertained.

KEY WORDS — auditory evoked potentials, brain stem potentials, middle ear surgery, sound probe.

INTRODUCTION

Success in reconstructive middle ear surgery usually cannot be judged before removing the packing of the ear canal at 2 or 3 weeks after the operation. An intraoperative estimation of hearing could facilitate decisions in the surgical procedure. Therefore, it would be advantageous to check the integrity of the ossicular chain in addition to its mechanical mobility.

The first attempts at intraoperative audiometry were carried out by Zöllner[1] and by Thullen.[2] They used an electrodynamic sound probe for stimulation, and the patient, under local anesthesia, had to detect the hearing threshold. This subjective method is not suitable for routine use, because an operating room is rather noisy, and because the patient often does not react predictably because of sedative drugs. When general anesthesia is required, no subjective audiometry can be performed.

To provide an objective method, brain stem evoked response audiometry (BERA) was established. Brain stem potentials are very reproducible, even under general anesthesia and various sedative drugs,[3] and have been applied successfully for monitoring vital functions in neurosurgery.[4,5] Wave V can be used for determining very closely the degree of conductive hearing loss.[6] The early application of brain stem potentials in ear surgery[7,8] revealed that stimulation by air conduction was not applicable when the middle ear cavity was opened, because the sensitivity is poor and the site of stimulation cannot be selected. Sound energy may be transmitted through both the oval and the round windows, bypassing the ossicular chain. Therefore we developed a piezoelectric transducer, the tip of which could be placed on various positions on the ossicular chain, allowing brain stem potentials to be recorded to click stimulation.[9]

The purpose of the present study was to improve the piezoelectric transducer, to determine the reliability of the method, to differentiate among various kinds of ossicular chain fixation, and to measure sound transmission through the newly constructed chain.

METHODS AND MATERIALS

In contrast to normal BERA, in which the patient is the main source of electric "noise," the major problem in the operating room is contamination by technical artifacts. Our measurements were carried out in an operating room with electrical shielding that greatly reduced the influence of external electromagnetic fields. The interior of an operating room, however, still contains quite a large number of indispensable electrical devices (the overhead operating light, microscope light system, cooling fans, electrocautery equipment, ECG monitor, video monitor, etc), the electromagnetic fields of which may be picked up by the recording electrodes. Furthermore, multiple grounding of the patient, eg, by accidental contact to metal parts of the operating table, has to be avoided. The EEG preamplifier must have a common mode rejection of at least 110 dB. Under adverse conditions, even the insertion of a power frequency suppression filter does not completely eliminate contamination of the response. With general anesthesia, needle electrodes were used and electrode impedance generally approximated 1 kΩ. In the rare cases of local anesthesia, silver disc electrodes had to be attached, which caused less stability and higher impedance (about 5 kΩ), making the procedure more difficult.

Electrode positions were the vertex (positive), the contralateral mastoid (negative), and the forehead for grounding.

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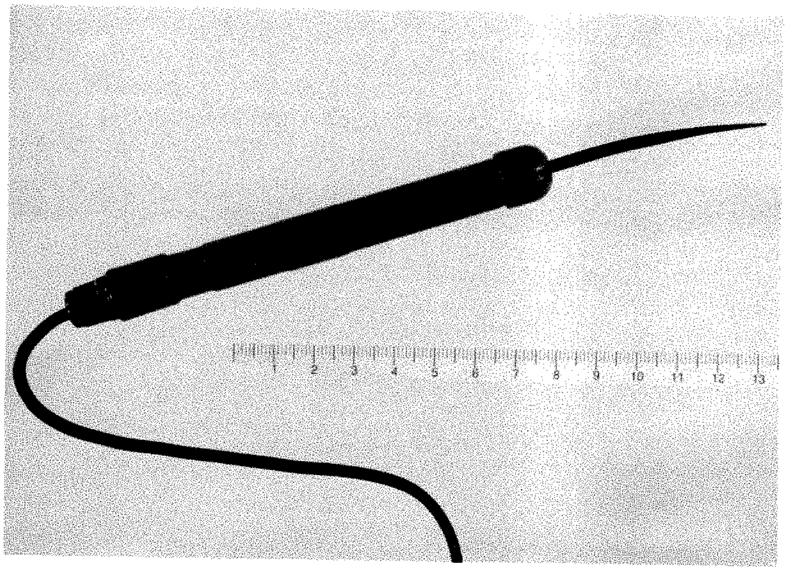

Fig 1. Piezoelectric transducer with bent sound probe for acoustic stimulation of ossicular chain. Scale is in centimeters.

The EEG was amplified with a flat gain between 20 and 1,500 Hz (filter slopes of 12 and 48 dB/octave). The analog-to-digital conversion rate was 10 kHz. Averaging was performed only while the surgeon was pressing a foot switch during stable stimulus conditions. The average of up to 2,000 sweeps was stored on a floppy disk and displayed on a CRT for the wave V latency readout. The other peaks were neglected, as they were much smaller, and neurologic differentiation was not required. Peak I would be missing in any case, because of the contralateral position of the reference electrode.

For stimulation of the ossicular chain, a piezoelectric transducer was applied (Fig 1). It consists of a pencil-like handle with a slightly bent plastic probe, the length of which is about 6 cm. The column of piezo plates contained in the handle is acoustically damped by an epoxy resin coating with grid wire for electrical shielding. The transfer function was leveled to a 5-dB ripple by damping and by mechanical antiresonators. Thus, the probe can deliver the biphasic click with only a small succeeding oscillation. Sound calibration was performed in a psychophysical experiment. The eardrum of a young volunteer with normal hearing was anesthetized. He determined the masking levels of white noise for a calibrated click delivered by a loudspeaker and by the piezo sound probe when positioned on the eardrum.

For the acquisition of brain stem potentials during middle ear operations, a click intensity of 90 dB normal hearing level (nHL) (117 dB peak equivalent sound pressure level) was applied in order to exceed environmental noise and to produce well-shaped potentials without the risk of damaging hair cells. The interstimulus time was 24 ms plus a random interval of up to 5 ms.

Most of the patients had suffered from chronic otitis media. In 11 cases tympanoplasty type I was performed, and in 27 cases type III procedures were done. If possible, brain stem potentials were measured at three points in the course of the operation:

1. Before opening the tympanum, with the probe positioned on the handle of the malleus.
2. In the cases of type III tympanoplasty, after removal of the incus remnant and resection of the head of the malleus, with the probe on the head of the stapes, or directly on the footplate in the few cases of missing superstructure of the stapes.
3. At the end of the operation, after positioning an ossicular prosthesis (autogenic, allogenic, or alloplastic [partial or total ossicular replacement prosthesis]), with the probe either on the prosthesis or on the handle of the malleus after closing of the eardrum.

To determine conductive hearing loss during the operation, wave V latency was evaluated. In contrast to amplitude, latency is very stable, and interindividual latency differences are small.[6,10] The conductive hearing loss can be determined by the latency delay attributed to the loss of intensity in the middle ear. In the latency/intensity diagram an intensity difference for a given latency shift can be determined as the horizontal distance to the mean latency function (Fig 2). In our diagram this function is linearized by appropriate latency scaling in order to facilitate the readout of conductive hearing loss.

RESULTS

Reproducibility of Stimulation by Sound Probe. First of all, we had to prove that mechanical stimulation of the ossicular chain by the piezoelectric transducer could evoke wave V with reproducible latency. For this purpose, measurements with re-

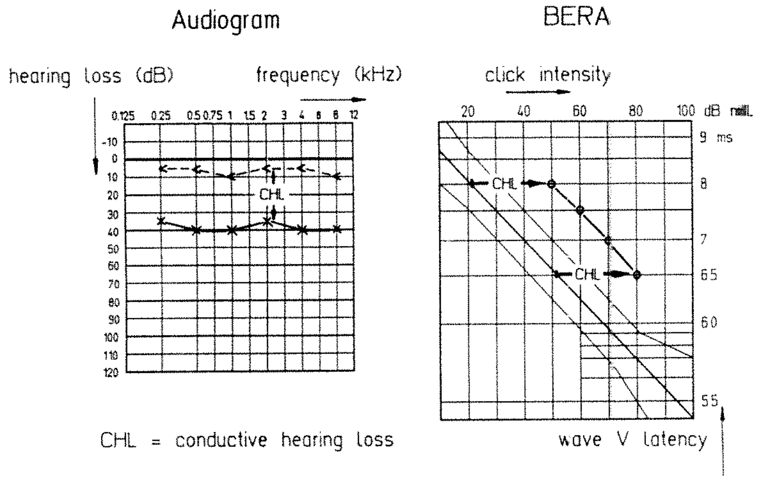

Fig 2. Determination of conductive hearing loss by brain stem wave V latency evaluation. Latency is delayed compared to normal (mean ± SD) values by amount corresponding to intensity reduction due to middle ear damage. BERA — brain stem evoked response audiometry.

peated positioning of the probe tip were performed. Two results of such an examination are presented in Fig 3. Twelve times the probe was placed on the handle of the malleus. The intraindividual standard deviation of latency was 0.15 ms, which is less than the interindividual value with headphones (0.25 ms, left side of Fig 3). At the intensity applied, a latency difference of 0.15 ms corresponds to an intensity variation of less than 10 dB. For a probe stimulation on the head of the stapes in 12 different ears (right side of Fig 3), the interindividual variance is about the same as with headphones on normal ears.

Subjective Hearing Loss and Latency. The preoperative measurements served as a reference to estimate hearing improvement. At the beginning of the operation, before opening of the tympanic membrane, the sound probe was placed on the handle of the malleus. Peak V latency correlated well with preoperative conductive hearing loss (Fig 4) as determined by pure tone audiometry. For this comparison, the air-bone gaps at 1, 2, and 3 kHz were averaged in order to approximate the maximal energy region of the click.

After disarticulation of the ossicular chain (in cases of type III tympanoplasty) we placed the probe on the head of the stapes or, in some cases, very cautiously on the footplate itself, if there was no stapes superstructure left. As could be expected, latencies were quite short and independent of sensorineural hearing loss (Fig 5). The variance is rather small, though some audiograms show a high frequency hearing loss.

Latency Reduction and Hearing Improvement. After reconstructing the ossicular chain the success of the operation with respect to hearing improvement could be estimated by another latency value obtained by stimulation at the handle of the malleus. This latency was compared to the initial value for malleus stimulation, and it cannot be shorter than the value for stapes stimulation. In Fig 6 the latency reduction due to the operation is compared to the improvement of conductive hearing

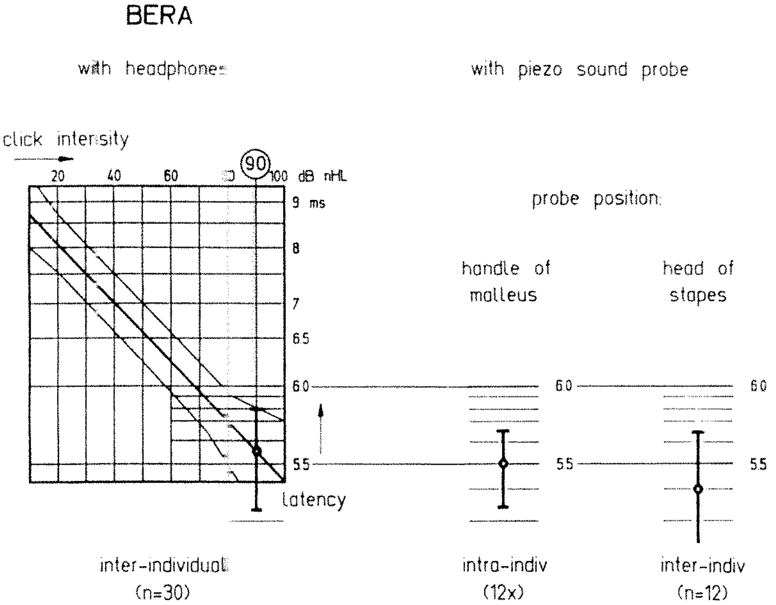

Fig 3. Reproducibility of wave V latency as produced by click stimulation at 90 dB normal hearing level. Interindividual latency standard deviation is about same for normal auditory response evoked by headphones (left side) and for mechanical stimulation of head of stapes by sound probe (right side). With intraindividual latency for probe position on handle of malleus, still smaller standard deviation is found (middle of figure). BERA — brain stem evoked response audiometry.

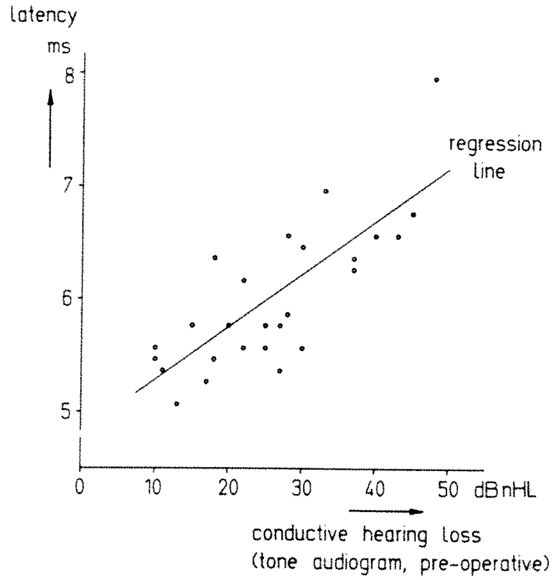

Fig 4. Good correlation of preoperative conductive hearing loss determined by pure tone audiometry (between 1 and 3 kHz) to latency for probe stimulation of handle of malleus at beginning of operation.

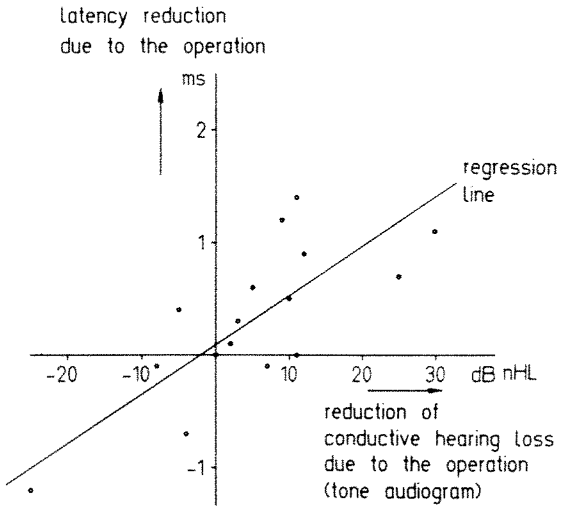

Fig 6. Operative success judged by pure tone audiogram (mean for 1, 2, and 3 kHz) 2 weeks after operation, in good agreement with latency reduction for probe stimulation of handle of malleus between beginning and end of operation.

loss as found in the pure tone audiogram 2 weeks later. The three negative values in cases of extensive cholesteatoma indicated the deterioration of hearing, which could not be avoided. Nevertheless, latency reduction and audiometric improvement of hearing correlated well.

Exemplary Cases. The practicability and significance of the procedure can be illustrated in two typical cases.

The preoperative audiogram of a 63-year-old man showed a high frequency drop-off and a 30-dB conductive hearing loss in the right ear (Fig 7). At the beginning of the operation a clear peak V with a latency of 5.4 ms was evoked by malleus stimulation. When the probe was placed on the stapes, a much shorter latency (4.9 ms) was found. After interposition of the autologous incus between the stapes and the malleus, a rather poor brain stem response was found, indicating insufficient sound transmission through the new ossicle (bottom of Fig 7). Thus the graft was replaced by a longer prosthesis. Now a clear peak V developed, the latency of which was nearly as short as it had been for stapes stimulation. The postoperative audiogram revealed a distinct improvement of hearing with a fairly reduced conductive hearing loss of 15 dB.

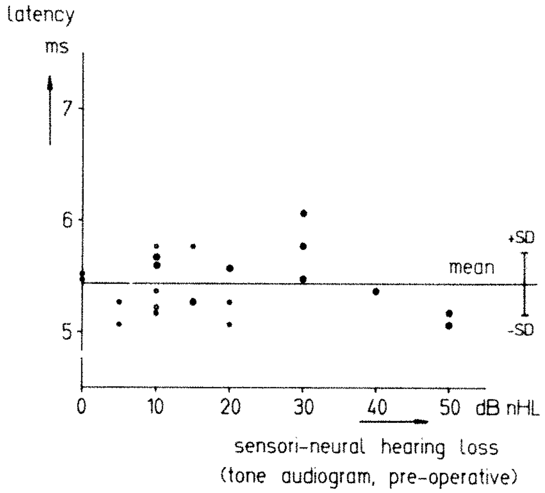

Fig 5. Preoperative sensorineural hearing loss determined by pure tone audiometry (mean for 1, 2, and 3 kHz) does not influence latency for probe stimulation of stapes. In cases of high frequency hearing loss (larger circles), slightly longer latencies are observed.

In the case of a 5-year-old girl the suspected fixation of the ossicular chain could be objectified and localized. Latency was 7 ms for stimulation of the handle of the malleus, corresponding to a conductive hearing loss of about 50 dB (Fig 8, diagram). For probe placement on the incus, the latency was normal (5.5 ms). Thus a fixation of the head of the malleus was confirmed.

DISCUSSION

We have attempted to demonstrate that the mechanical stimulation of the ossicular chain by a piezo sound probe can be performed as accurately as usual acoustic stimulation by headphones. Wave V latency yields about the same reproducibility, and changes of conductive hearing loss can be estimated with an accuracy of 5 to 10 dB. The absolute amount of conductive hearing loss is slightly less determinable, owing to the greater interindividual variance. The audiometric air-bone gap correlated closely with the latency delay. A moderate sensorineural hearing loss does not influence latency at high stimulus levels.[6] Even a profound high fre-

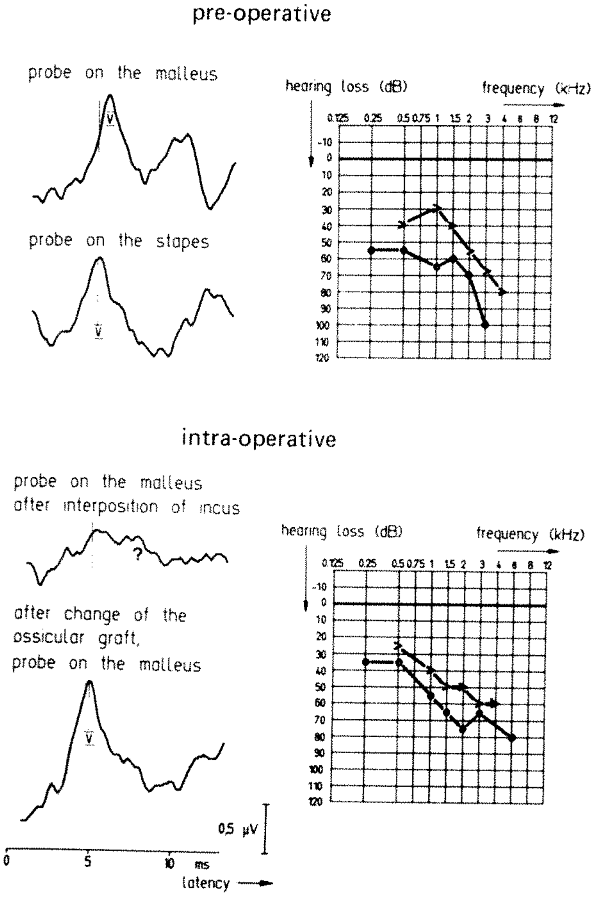

Fig 7. Example of intraoperative audiometry used for control of ossicular graft function with brain stem potentials recorded for different probe stimulation sites. Insufficient sound transfer of incus initially interposed (question mark) was affirmed and could immediately be amended.

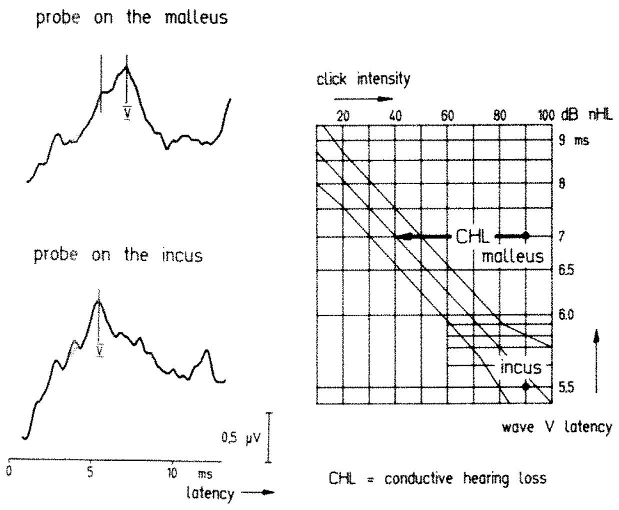

Fig 8. Example of intraoperative objectification of head-of-malleus fixation. Latency is delayed according to audiometric conductive hearing loss for probe stimulation of malleus, and it is quite normal when incus is stimulated.

quency hearing loss that would delay latency at low stimulus intensity because of cochlear travelling time does not affect the results, because at 90 dB nHL loudness recruitment is reached in most ears. There is no risk of hair cell damage, as this intensity is applied only for a short time.

The success of a middle ear operation usually is judged by preoperative and postoperative pure tone audiometry. The reduction of conductive hearing loss corresponds well to intraoperative latency differences for malleus stimulation, before tympanotomy and after reconstruction of the ossicular chain. Some deviation between the intraoperative prognosis and the subjective result — which is obtained about 2 weeks later — may be caused by the postoperative healing process. However, this fact does not reduce the practical importance of testing middle ear function intraoperatively. A minimal latency (down to the value for stapes stimulation) indicates optimal sound transfer. Thus, the recording can be used for optimizing ossicular placement.

The prognosis of hearing improvement by latency differences can only be accurate if the absolute latency value is regarded. Because of the nonlinear dependency of latency on click intensity (as evidenced by the almost logarithmic latency scale in Fig 2), a measured latency difference indicates a higher difference of hearing when produced at a lower intensity level, or at a higher conductive hearing loss, as the inner ear receives less energy when the conductive hearing loss is greater.

From the clinical point of view the method is fully developed for routine use. Intraoperative audiometry cannot be required, however, as an indispensable requisite of standard middle ear surgery. The experienced surgeon will certainly keep relying on his practical experience and his tactile sense, particularly since intraoperative audiometry requires some additional effort and expense. However, intraoperative audiometry can refine the techniques of younger ear surgeons. Its most important achievement, however, is to provide help in situations in which the tactile sense and experience of the surgeon are not sufficient to estimate either the exact site of disturbance or the correct position of replaced ossicles. Consequently, intraoperative audiometry should be done preventively in those cases in which a possible deviation from routine surgery is expected. The conventional approach is to base the decision upon preoperative subjective audiometry and the mobility of the ossicles as judged during surgery. In the following situations, intraoperative audiometry may be helpful: fixation of the head of the malleus, some cases of tympanosclerosis, partial fracture of the crura of the stapes, and limited view of the oval and/or round windows. Intraoperative clarification is especially important, as a completely different surgical procedure is required for an otosclerotic fixation of the stapes than for a fixation of the head of the malleus.

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THE DEAFNESS RESEARCH FOUNDATION OTOLOGICAL RESEARCH FELLOWSHIP FOR THIRD YEAR MEDICAL STUDENTS

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SALIVARY GLAND CARCINOSARCOMA: TRUE MALIGNANT MIXED TUMOR

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True malignant mixed tumor, or carcinosarcoma, of salivary gland origin is rare. Only 19 cases have been reported in the literature, and a review of cases seen at the University of Iowa over the last 60 years yielded only two. In one case the mesenchymal component of the tumor contained both osteosarcoma and chondrosarcoma. In the second case, the history and the histology suggest a progression from a carcinoma ex pleomorphic adenoma to a carcinosarcoma. These features are documented in this report and literature review.

KEY WORDS — carcinosarcoma, malignancy, salivary gland.

CASE REPORTS

Case 1. The patient, a 57-year-old woman, was first seen at the University of Iowa Hospitals and Clinics on July 9, 1985, for a left facial mass that began as a small papular growth near the left zygoma. The mass was first noticed by the patient in November 1984. It enlarged and the patient experienced left facial paralysis, which was noted in May 1985. By July, the mass had become purulent and infested with maggots, and the patient sought medical attention.

The patient reported no history of a parotid mass prior to the present illness, although she had experienced a recent 7-kg weight loss. The fungating left facial mass extended from just below the mandibular angle inferiorly to the top of the pinna superiorly and from the lateral canthus to behind the external auditory canal (Fig 1A). Examination revealed no palpable lymphadenopathy. X-ray studies showed no pulmonary metastases.

The tumor was resected in a staged procedure involving a left parotidectomy, radical neck dissection, lateral temporal bone resection, lateral maxillectomy, lateral orbital wall resection, hemimandibulectomy, lateral tarsorrhaphy, full mouth tooth extraction, and reconstruction of the face using the latissimus dorsi myocutaneous flap with a split-thickness skin graft to the open back wound. The pathologic diagnosis was true malignant mixed tumor of salivary gland origin.

Within 6 weeks postoperatively, extensive local tumor recurrence accompanied by wound infection was apparent. The patient also had extreme metabolic acid-base imbalance and seizure activity associated with a new hypodensity in the left temporal region observed on computed tomography. She died on Aug 26, 1985. A postmortem examination was performed.

Microscopic study of the original resected tissue revealed a biphasic malignancy associated with a benign mixed tumor. The remnants of the benign tumor were composed of epithelial cellular strands and small glands in a myxoid stroma. The malignant elements included cells with myoepithelial characteristics (plasmacytoid and fibroblastic features) as well as areas of ductal carcinoma. Necrosis was common in these latter epithelial areas. The most interesting sarcomatous feature was the presence of osteosarcoma. Figure 1B shows malignant cells abutting and embedding in an osteoid matrix. The foci of osteosarcoma were scattered widely throughout the neoplasm but were associated generally with chondrosarcomatous areas (Fig 1C), which were predominantly grade 2. Other malignant sarcomatous components were present but did not show clear differentiation toward other recognizable sarcomas, eg, fibrosarcoma or malignant fibrous histiocytoma. Neither perineural nor lymphatic invasion was seen.

At autopsy, tumor was found in the sella turcica and right cavernous sinus. There appeared to be no direct connection between these latter sites and the primary site of the tumor (left parotid). Pulmonary and hilar metastases were identical to the primary tumor, including the presence of osteosarcoma with areas of carcinoma and undifferentiated sarcoma. No other metastases were seen.

Case 2. The patient, a woman 59 years of age, first presented with a right submaxillary mass. A

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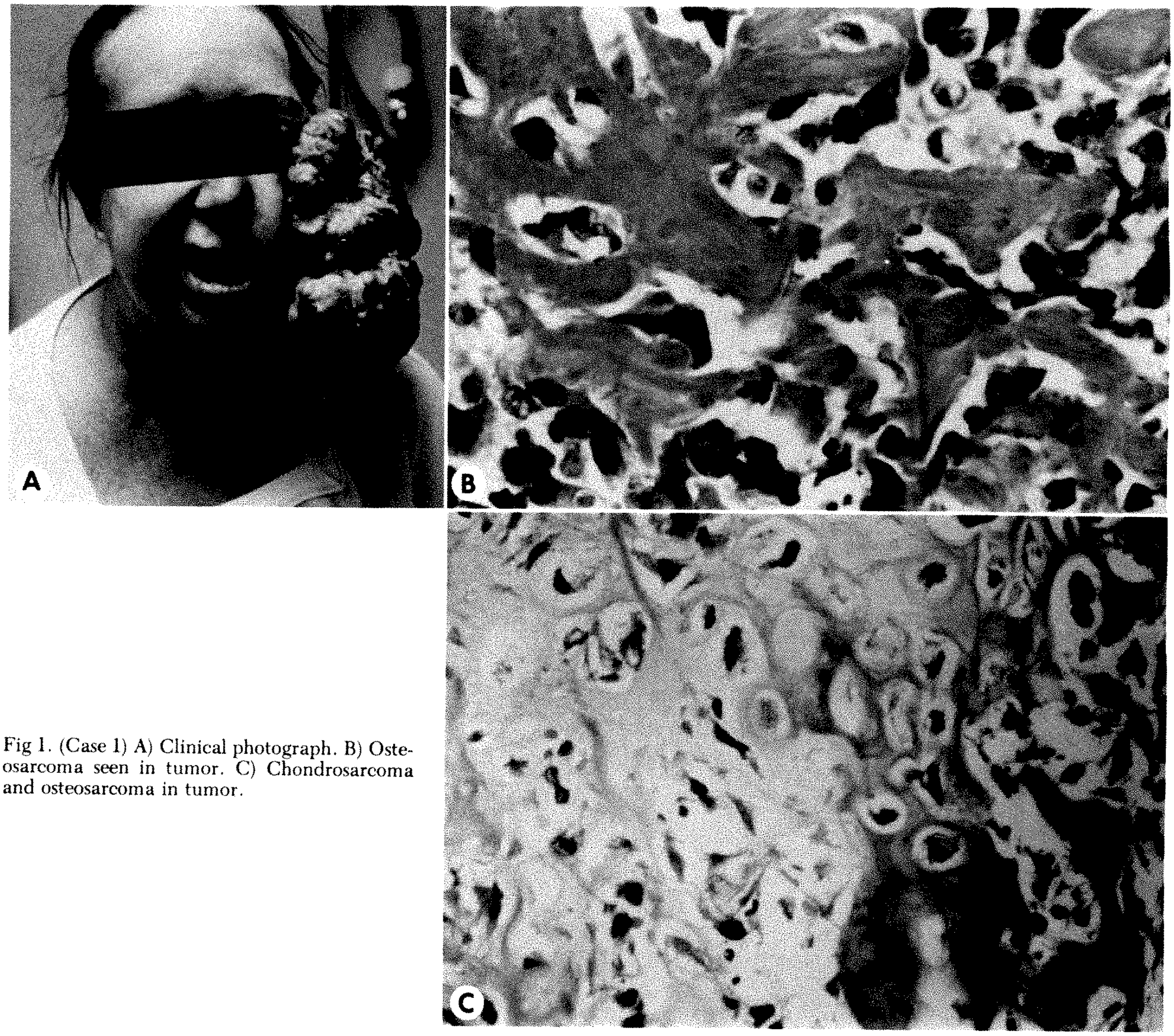

Fig 1. (Case 1) A) Clinical photograph. B) Osteosarcoma seen in tumor. C) Chondrosarcoma and osteosarcoma in tumor.

tumor was found in the posterior aspect of the submaxillary gland and was excised with the gland. Thirteen months later the patient returned with a right infrahyoid mass. At surgery, a recurrent tumor was found adhering to soft tissue and bone. The patient underwent a composite resection with a modified radical neck dissection. Metastatic disease was found in a single lymph node. She received postoperative radiation therapy, but returned in 8 months with severe facial pain. Biopsy showed recurrent tumor, and the patient declined a mandibular resection. Six months later she returned with gross tumor involving the mandible and floor of mouth. Two different chemotherapy regimens produced no response. In March 1986, she was referred to the University of Iowa Hospitals and Clinics for evaluation. On the basis of physical examination and CT, we judged the tumor unresectable. The patient died of disease 12 months later. A postmortem examination was not performed.

Microscopic sections of the first resection showed a tumor with a myxoid stroma within which were embedded benign-appearing epithelial cell clusters. In some areas, however, the epithelial cells showed increased nuclear size and occasional mitotic figures. In the second resection a marked cytologic change was evident. Much of the tumor showed epithelial clusters that had malignant cytologic features and were characterized by amphophilic cytoplasm and large hyperchromatic nuclei and frequent mitoses. Necrosis of these epithelial clusters was present (Fig 2A). Although some of the myxoid and cartilaginous stromal cells associated with the malignant epithelium did not show atypia, several areas of unequivocal chondrosarcoma, grades 1 and 2, were present (Fig 2B).

DISCUSSION

The term malignant mixed tumor of salivary gland origin often is used synonymously with carcinoma ex pleomorphic adenoma, as the latter comprises nearly 99% of these neoplasms.[1] Two other

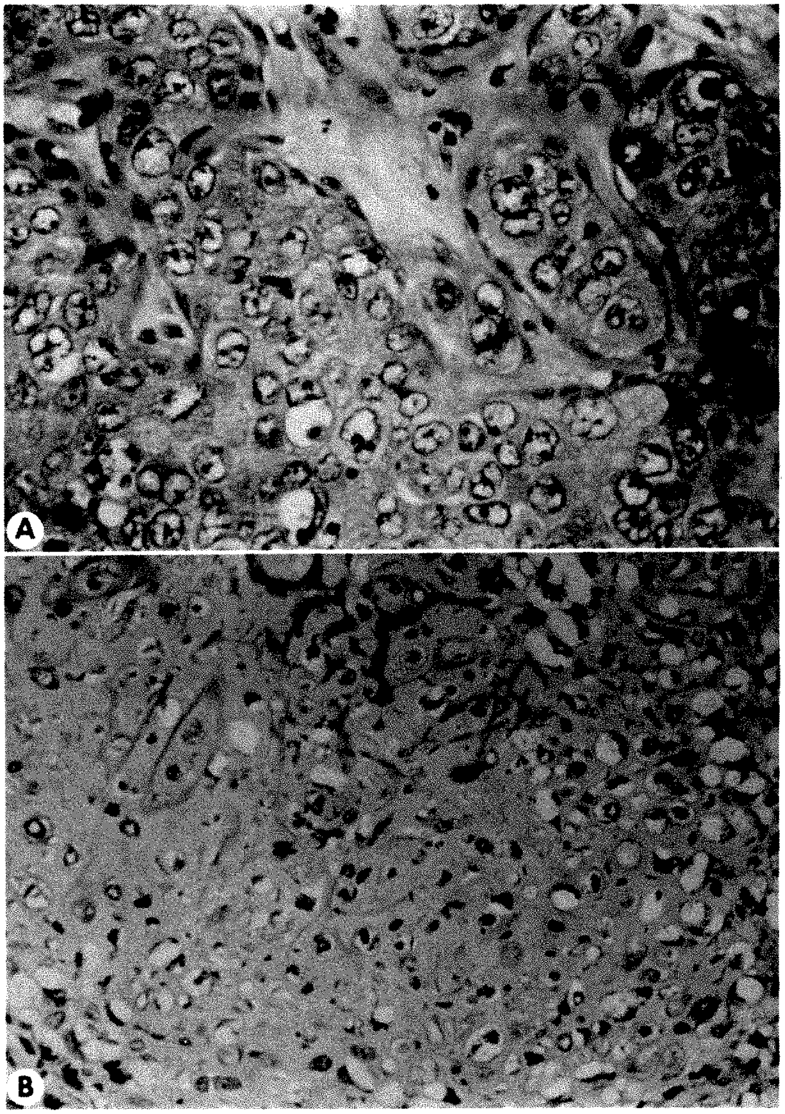

Fig 2. (Case 2) A) Malignant epithelial component in tumor. B) Area showing predominantly chondrosarcomatous portion of tumor.

histologic variants have been described. One is a mixed tumor with distant metastases in which tissue at both sites has a histologically benign appearance. Only eight such cases were reported in the literature through 1978.[2] The third variant is a carcinoma or true malignant mixed tumor[3] and contains malignant tissues of both epithelial and mesenchymal histologic types. Although elements of both chondrosarcoma and osteosarcoma have been seen separately,[4,5] our report is the first of a true malignant mixed tumor of salivary gland origin in which the mesenchymal component contained both chondrosarcoma and osteosarcoma.

The limited published information available on true malignant mixed tumors is summarized in the Table.[4-7] Lack of uniformity among reports and a small number of cases preclude statistical analysis, but some generalizations may be made. These are tumors occurring in midadult life, commonly in the sixth decade, and there is female predominance. Long-term survival (>5 years) is unusual. The primary tumor site most often is a major salivary gland with only one reported exception; the parotid gland is the single most common site. As might be expected, the malignant epithelial tissue type usually is adenocarcinoma. Chondrosarcoma is the predominant mesenchymal histologic type.

Our two cases correspond with those previously reported in the literature with respect to the presence of hematogenous metastases, a low incidence of nodal metastases, and the presence or history of pleomorphic adenoma.[4]

Our cases are consistent with the concept that malignant mixed tumors of salivary gland origin represent a point on a continuum of neoplasia rather than an isolated tumor class. Malignant changes in pleomorphic adenomas may occasionally supervene, and in the individual patient the possible consequences of nonoperative management are to be weighed against the known risks of surgical treatment.

REPORTED CASES OF SALIVARY GLAND CARCINOSARCOMA

Reference	*Age*	*Sex*	*Site*	*Carcinoma*	*Sarcoma*	*Other*
Stephen et al[4] (12 patients)	Mean, 55 yr	2:1 F:M	Nine parotid, two submaxillary, one minor (palate)	Twelve ductal adenocarcinoma, two also with undifferentiated carcinoma, one also with squamous cell carcinoma	Ten chondrosarcoma, two fibrosarcoma	Eight recurrences, six metastases (two nodal), six dead of disease at 3.6 yr mean, six alive. (Of these latter six, two had recurrences < 1 yr, two died of other causes but free of disease at 2 and 17 yr, one alive 4 yr with recurrence, one alive < 1 yr with recurrence.) Six had prior benign mixed tumor.
Chen et al[5]	59 yr	F	Parotid	Adenocarcinoma and squamous cell carcinoma	Osteosarcoma	Dead of disease 7 mo, palpable nodes before death. No evidence of benign mixed tumor.
NCI monograph[6]	X	M	Major	X	X	X
	X	F	Major	X	X	X
Kirklin et al[7]	X	X	Parotid	Adenocarcinoma	X	Dead of disease < 1 yr (no nodes)
	X	X	Parotid	Adenocarcinoma	X	Dead of disease < 6 yr (no nodes)
	X	X	Parotid	Adenocarcinoma	X	Alive 19 yr postop (no nodes)
	X	X	Parotid	Squamous cell carcinoma	X	Dead of disease < 2 yr (no nodes)
This study	57 yr	F	Parotid	Adenocarcinoma	Chondrosarcoma, osteosarcoma	Metastases, recurrence, dead of disease < 1 yr; also benign mixed tumor tissue
	59 yr	F	Submaxillary	Undifferentiated carcinoma	Chondrosarcoma	Recurrence, nodes, benign mixed tumor tissue; dead of disease < 3 yr

X — data not available or could not be reconstructed from case report.

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FETOR FROM ULCERATED HEAD AND NECK TUMORS: CAUSATION AND THERAPY

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Almost all extensive tumors of the head or neck generate a fetor very unpleasant for the patient, his family, and the nursing staff. Thirty-one patients suspected of having a microbial superinfection of the tumor masses caused by anaerobes or an aerobe-anaerobe mixed infection were examined, and tumor samples from the oral cavity, throat, and larynx were obtained. Anaerobes could be demonstrated in every case, especially *Bacteroides melaninogenicus*. In the antibiotic treatment, clindamycin (Cleocin) proved to be superior to metronidazole (Clont). Within 12 to 24 hours after initiation of treatment, at the most 36 hours, the fetor almost always disappeared. The odor was stopped as long as antibiotic therapy continued.

KEY WORDS — anaerobic bacteria, fetor, head and neck tumor, ulcer.

INTRODUCTION

Practically every otolaryngologist has had experience with patients suffering from exophytic or ulcerated tumors or recurrent tumors of the head or neck (see Figure). In such cases, palliative measures are necessary to prolong and improve the quality of life of the patient. In addition to the palliative tumor therapy, food intake and respiration as well as alleviation of pain also must be assured. Ulcerated tumors frequently emit a putrid odor that considerably limits the patient's social contacts, since the unpleasant odor can be so intense that the patient is no longer visited by his family and the nursing staff performs only the most necessary measures. The strong stench is often responsible for the additional isolation of the very ill patient in the terminal phase of the illness. Infections associated with fetid odor may be induced by anaerobic bacteria. That the odor emitted from ulcerated tumors is caused by anaerobes is therefore very probable.[1,2]

NORMAL HABITAT OF ANAEROBES

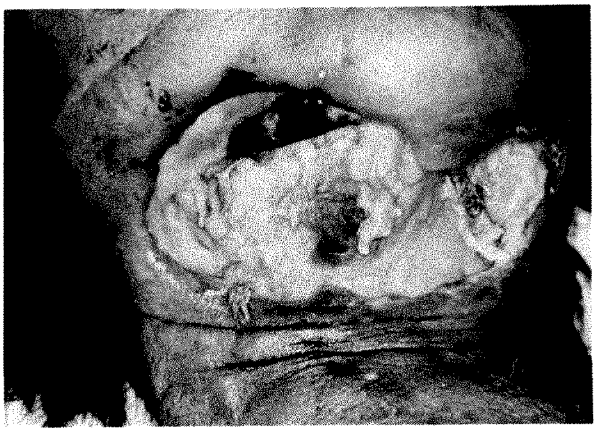
Anaerobes greatly outnumber aerobes in the oropharyngeal, intestinal, and cutaneous bacterial flora of humans.[3] The normal flora of the mouth and throat is composed primarily of anaerobes.[3] They are 30 times more frequent in this region than aerobic bacteria.[4] *Veillonella* and *Peptostreptococcus*, for example, are frequently found in saliva. *Bacteroides melaninogenicus* is particularly common in the alveolar pockets and is often responsible for bad breath (fetor ex ore).

PREDISPOSITION TO ANAEROBIC INFECTIONS

Factors that can lead to anaerobic infections through lowering of the oxygen partial pressure include tissue acidosis, necrosis, gangrene, edema, and neoplasms. In addition, corticosteroid and immunosuppressive therapy are predisposing factors.[4-6]

ANAEROBIC HEAD AND NECK INFECTIONS

According to the otorhinolaryngologic and oral surgical literature, about 20 different types of head and neck infections are caused wholly or primarily by anaerobes. Anaerobic bacteria are present in numerous cases of otitis media.[1,7,8] The presence of anaerobes should be considered, especially in cases of chronic otitis media. *Bacteroides fragilis* occurs regularly in otogenic brain abscesses. Acute otitis media and mastoiditis may also be caused by anaerobes, even though pneumococci, *Streptococcus pyogenes*, and *Staphylococcus aureus* play a particularly important role. However, anaerobes such as *Fusobacterium*, *Peptostreptococcus*, and *Bacteroides* are important causes of chronic sinusitis.[7]



Recurrence of carcinoma of floor of mouth with greasy ulcer. Fetor was due to anaerobic superinfection.

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Peritonsillar abscesses are typical anaerobic infections, as demonstrated by the considerable fetor after abscess incision or abscess tonsillectomy. Anaerobes can be demonstrated routinely in chronic tonsillitis.[9] Fusobacteria are almost always present in Plaut's angina and Vincent's angina.[4] The presence of anaerobes is etiopathologically certain in Ludwig's angina.[1,6] Cervicofacial actinomycosis is an aerobic-anaerobic mixed infection.[7] Anaerobes also play an important role in throat abscesses. They also must be considered as possible pathogens in collar mediastinitis of the neck. Anaerobes rarely are found in acute suppurative parotitis. *Bacteroides* sp, *Fusobacterium*, and *Peptostreptococcus* also have been found in orbital phlegmons. Dental alveolar abscesses are typical anaerobic infections. Anaerobes usually are present in periodontitis and chronic pulpitis.[4] Anaerobic infections after tumor surgery in the head and neck region must be considered especially in diabetics. Healing in the mouth and face regions may be complicated by anaerobes.

IDENTIFICATION OF ANAEROBIC INFECTIONS

Particularly if mucous membrane infections, necrotizing soft tissue infections, and neoplasms constitute the basic illness, anaerobic infections usually are involved, especially if the infection is accompanied by a putrid odor. Also, so-called sterile pus may be an indicator of anaerobic and not of aerobic involvement.[6] The presence of anaerobic bacteria is not demonstrated readily, since they are rapidly killed off by atmospheric oxygen. For this reason, it is best to examine tissue samples rather than surface smears. Care should be taken that bacteria are not killed off by atmospheric oxygen during transport. Therefore, the sample must be transported in a special nutrient-rich, reduced medium that prevents bacterial exposure to oxygen. In addition, the bacteriologist must employ special fluorescence serologic and gas chromatographic methods. Since these methods are not always routinely used in microbiology, the bacteriologist must be advised that an anaerobic infection may be involved.

STUDY

In the past 4 years, 31 patients with extensive tumors of the nasopharynx (one patient), oropharynx (11 patients), and hypopharynx (six patients) as well as of the oral cavity (six patients) and larynx (seven patients) that gave off a putrid odor were treated. In some cases, these were incurable recurrences. The odor could be controlled only minimally by intensive local therapy with antiseptic solutions and frequent changes of dressing. In order to determine the cause of the putrid odor, bacteriologic examinations were performed either on smears from the ulcerating tumors or on samples of the tumors themselves. The bacteriologic examinations were performed at the Institute of Hygiene of the University of Cologne.

MICROORGANISMS IN ULCERATED TUMORS ($N = 31$)

Organism	*No. of Isolates*
Anaerobes	
Bacteroides melaninogenicus	25
Bacteroides oralis	15
Peptococci	12
Bacteroides bivius	10
Gram-negative *Bacteroidaceae*	8
Fusobacteria	8
Peptostreptococci	4
Aerobes	13

In every case, a large microbial population in the tumor masses was demonstrated. Distinct populations of anaerobes always were present. In most cases, several anaerobe species were demonstrated (total of 82 isolates). Anaerobe-aerobe mixed infections were present in 13 cases. Aerobes were never exclusively present in the tumor masses.

The most frequently demonstrated microorganism was *B melaninogenicus* (25 cases), followed by *Bacteroides oralis* (15 cases), *Peptococcus*, and *Bacteroides bivius* (see Table). In most cases, the putrid odor was caused by *B melaninogenicus*. This organism or its fatty acids and their metabolic products are responsible for the fetid odor. Predicting that the fetid odor would disappear if the anaerobes were kept in check, we initiated a specific antibiotic therapy. Clindamycin hydrochloride (Cleocin HCl) and metronidazole (Clont) are the most effective antibiotics against all *Bacteroides* species.[10] With the administration of clindamycin (two 150-mg Cleocin capsules four times per day) or metronidazole (one 250-mg Clont tablet five times per day), the fetor disappeared in almost all cases. In only two cases was fetor still weakly detectable in spite of antibiotic therapy. Sixteen patients were treated with clindamycin, and 15 patients with metronidazole. The fetor disappeared more quickly after treatment with clindamycin than with metronidazole. Localization of tumor had no influence on the result of treatment. Side effects of the drugs were not observed. Surprisingly, the fetor was completely gone after 12 to 24 hours, at most 36 hours, after initiation of therapy. At the same time, it could be bacteriologically demonstrated that anaerobic organisms simultaneously disappeared in the tumor.

Anti-anaerobic therapy cannot influence the tumor itself. The very annoying accompanying fetor, however, can be checked effectively in almost every case. But the drug therapy must be long-term, since the termination of therapy soon would lead to a renewed anaerobic or aerobic infection of the tumor as well as strong fetor.

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THE SIXTH WORLD CONGRESS FOR BRONCHOLOGY

The Sixth World Congress for Bronchology will be held October 18-20, 1989, in Tokyo, and October 20-22, 1989, in Kyoto, Japan. For further information, contact Dr Masayuki Niitsuma, Secretary General, 6th World Congress for Bronchology, Department of Surgery, Tokyo Medical College, 6-7-1 Nishishinjuku, Shinjuku-ku, Tokyo 160, Japan; telephone 03-342-6111.

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The Conference on the Eustachian Tube and Middle Ear Diseases will be held October 26-29, 1989, in Geneva. For further information, contact Prof Jacob Sade, Chairman, c/o The Secretariat, Conference on the Eustachian Tube and Middle Ear Diseases, Intercontinental Hotel Geneva, 7-9 CH du Petit Saconnex, CH-1211 Geneva 19, Switzerland.

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LARGE PITUITARY ADENOMAS WITH EXTENSION INTO THE NASOPHARYNX

REPORT OF THREE CASES WITH A REVIEW OF THE LITERATURE

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Three cases of pituitary adenoma with extension into the nasopharynx and nasal cavity are reported. The occurrence of this rare tumor underscores the need to consider a pituitary tumor whenever a patient presents with rhinologic complaints and destruction of the sellar floor. Epistaxis, although exceptional, may be the first manifestation of a pituitary tumor. Immunohistochemical analysis combined with staining for the pituitary hormones proved to be essential for reaching a definite diagnosis. Magnetic resonance imaging seems to be the modality of choice for differentiation between tumorous and nontumorous sinus obstruction.

KEY WORDS — epistaxis, extracranial extension, immunohistochemical analysis, magnetic resonance imaging, nasopharynx, pituitary adenoma, prolactinoma.

INTRODUCTION

Pituitary adenomas with extension into the nasopharynx and nasal cavity represent a very uncommon situation that has remained unmentioned in general textbooks. A review of the literature yielded only 24 cases, most of them reported as case histories. On the basis of a number of larger series, the incidence of this very unusual type of infrasellar tumor extension was estimated to be about 2%.[1-3] In a large majority of the reported cases, the otolaryngic symptoms developed as a late tumor complication, and epistaxis occurred as the first symptom of a pituitary tumor in only five cases.[4-7]

This communication describes three patients with transsphenoidal extension of a pituitary tumor who initially seemed to have only a rhinologic problem, and points to the necessity to include both pituitary and otolaryngic neoplasms in the differential diagnosis of lesions that can destroy the base of the skull. It also addresses the question of the natural connection between the sphenoid sinus and the nasal cavity as a possible site of tumor penetration. The relative value of magnetic resonance imaging and computed tomography in estimating tumor extension is discussed.

CASE REPORTS

Case 1. A 54-year-old man was admitted to the otolaryngology department of our hospital with a severe nosebleed in the summer of 1985. For the last 2 years he had been complaining of frontal headache and left-sided nasal obstruction with intermittent rhinorrhea, and for the last 2 months had suffered from recurrent epistaxis. He also had been impotent for 6 years. On inspection, a bluish brown smooth tumor was seen in the left nasal cavity and the nasopharynx. Several specimens were taken for biopsy, which eventually led to the diagnosis prolactinoma.

Neurologic and ophthalmologic examination disclosed no abnormalities except a slight sixth nerve paresis of the left eye without diplopia. Neither visual fields and acuity nor evoked potentials were impaired. A plain film showed an enlarged sella with destruction of the sellar floor.

Axial and coronal CT scans (Fig 1) showed a sellar and suprasellar mass extending into the ethmoid and sphenoid sinuses, nasal cavity, and nasopharynx. The tumor was graded according to Wilson's modification of Hardy's classification as a grade IV B,D,E.[8,9]

The MRI pictures (Fig 2) revealed the same tumor extension and in addition showed a nontumorous involvement of the left maxillary sinus due to mucosal swelling.

Endocrine examination showed elevated serum prolactin levels (582 to 820 µg/L; reference, <12 µg/L), with a definite response to thyroid-stimulating hormone releasing hormone (1,500 µg/L) and to a single dose of 2.5 mg bromocriptine (160 µg/L). The other abnormalities included decreased serum testosterone (0.70 nmol/L; reference, 12.5 to 35), decreased gonadotropins without increase of luteinizing hormone releasing hormone, and abolished response of growth hormone to hypoglycemia.

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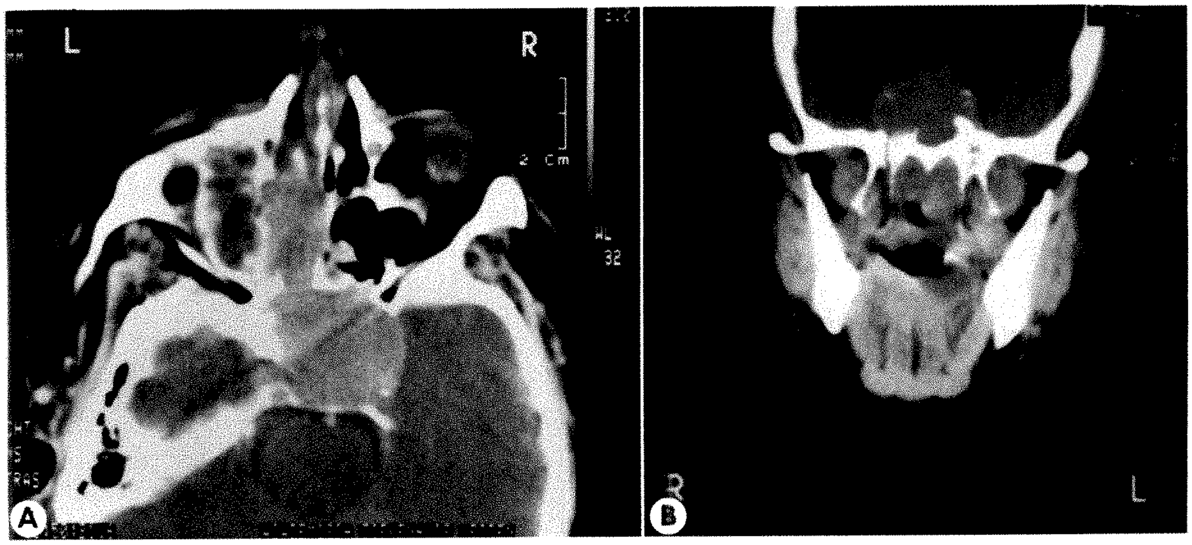

Fig 1. (Case 1) Computed tomographs. A) Transverse section showing extension of sellar mass into sphenoid sinus and left nasal cavity. B) Coronal section showing extension of parasellar and suprasellar masses. Floor of third ventricle is compressed by tumor.

After 4 weeks of bromocriptine therapy (5.0 mg tid), which reduced prolactin levels to 100 μg/L, the size of the tumor was unchanged. Therefore, tumor removal via a transseptal transsphenoidal approach was attempted. The infrasellar and intrasellar parts of the tumor could be removed completely, and tumor involvement of the left maxillary sinus was excluded. Despite use of the usual procedures to increase intracranial pressure during the operation, the suprasellar part of the tumor remained in situ and could not be removed safely via this approach. This failure was attributed also to the firmness of the tumor tissue. The large defect of the sellar floor was repaired by bone grafting. Postoperatively, the serum prolactin level remained elevated, and therefore bromocriptine therapy was resumed.

The biopsy specimens taken from the nasal cavity showed a stromal area with groups of small, round, regular cells (Fig 3). The nuclei were round and dark, and lay in a fine-granular eosinophilic cytoplasm. Atypia and mitotic figures were not seen. The initial differential diagnosis was esthesioneuroblastoma, undifferentiated carcinoma, or malignant lymphoma. Immunoperoxidase staining was performed with neuron-specific enolase (Dakopatts, Denmark), keratin, and common leukocyte antigen.

Since Gomori staining revealed a somewhat alveolar architecture that suggested the remote possibility of a pituitary tumor, the immunohistochemical analysis was extended to include staining for pituitary hormones. The tumor cells were stained positively by neuron-specific enolase. Keratin and common leukocyte antigen staining did not occur, hence undifferentiated carcinoma or lymphoid neoplasia was very unlikely. The finding that prolactin was present in the tumor cells, but not adrenocorticotropic hormone, growth hormone, or human chorionic gonadotropin, was considered sufficient evidence to permit the diagnosis of prolactin-containing pituitary adenoma. Tissue removed at surgery contained a large fragment of an easily identifiable pituitary adenoma with prolactin as the only hormone (Fig 4).

Although bromocriptine (up to 5.0 mg qid) reduced postoperative prolactin levels from 387 μg/L to almost-normal values (20 μg/L), no reduction of the tumor size was obtained. After 2 years the suprasellar tumor remnants appear to be unchanged. So far, additional radiation therapy has been withheld, because effective exposure of the ethmoidal tumor remnants can be expected to damage the visual pathways and compromise the patient's visual acuity.

Two and a half years after the operation, the patient is in good health without rhinologic complaints, CSF leakage, or other signs of tumor proliferation, and is on maintenance medication consisting of levothyroxine (0.1 mg/d), bromocriptine (22.5 mg/d), and testosterone undecanoate (40 mg tid).

Case 2. This 34-year-old man presented in 1985 with bilateral nasal obstruction of 2½ years' duration. There were no complaints of rhinorrhea or signs of pituitary dysfunction. A recent nasal septoplasty had not given permanent relief.

Plain x-ray films and tomography of the sella turcica region showed an enlarged sella with destruction of the floor and opacification of the sphenoid sinus. Computed tomographic scans revealed a sellar mass with suprasellar extension compressing the third ventricle and protrusion of the sphenoid mass into the nasal cavity, but no disruption of the sphenoidal boundaries (tumor grade IV, B,E[8,9]).

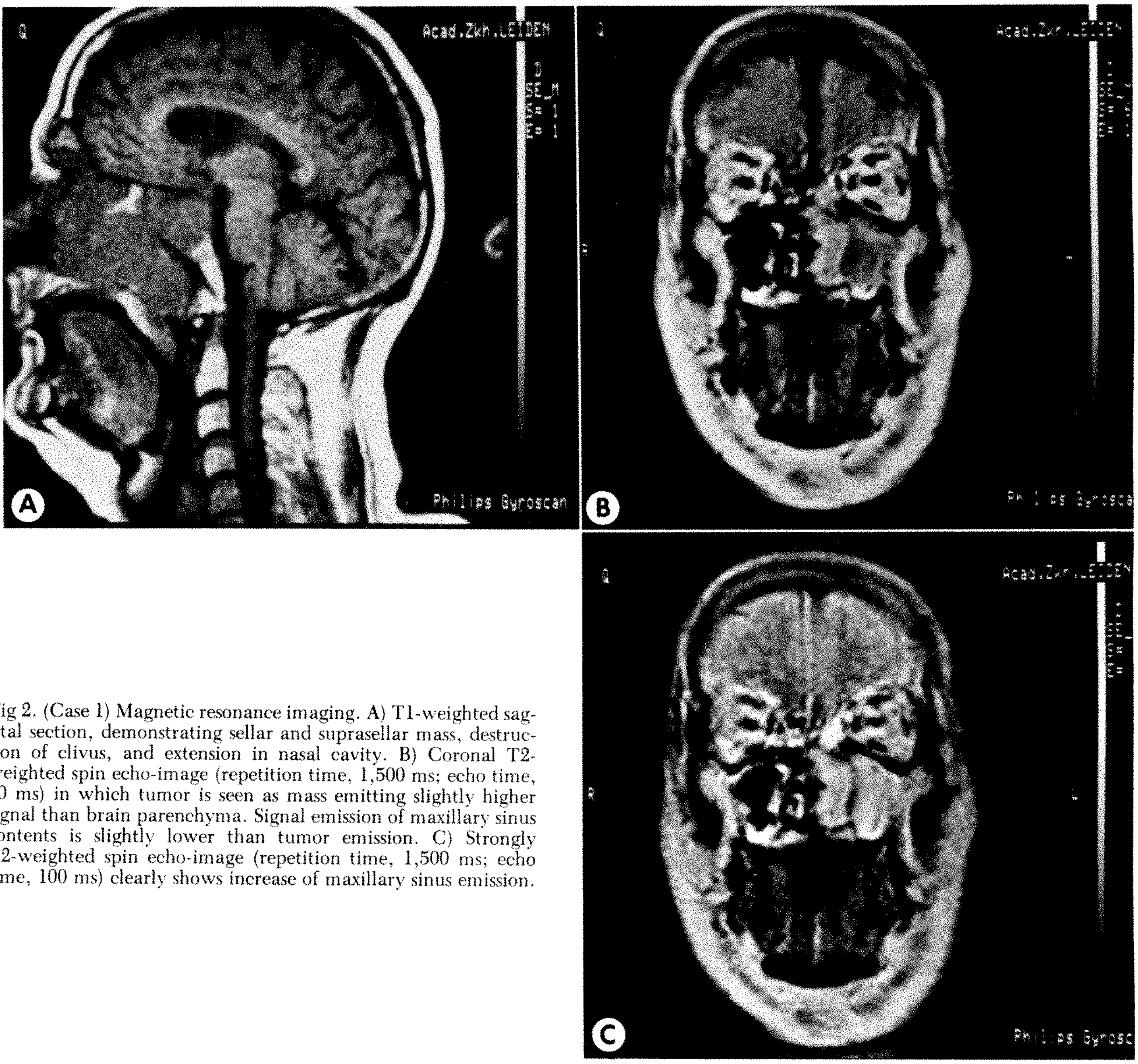

Fig 2. (Case 1) Magnetic resonance imaging. A) T1-weighted sagittal section, demonstrating sellar and suprasellar mass, destruction of clivus, and extension in nasal cavity. B) Coronal T2-weighted spin echo-image (repetition time, 1,500 ms; echo time, 50 ms) in which tumor is seen as mass emitting slightly higher signal than brain parenchyma. Signal emission of maxillary sinus contents is slightly lower than tumor emission. C) Strongly T2-weighted spin echo-image (repetition time, 1,500 ms; echo time, 100 ms) clearly shows increase of maxillary sinus emission.

Examination of the visual fields showed bitemporal hemianopsia and a slightly decreased visual acuity (ODS 0.8).

Endocrinologic examination revealed decreased serum testosterone (7.0 nmol/L) and decreased growth hormone reserve. The other pituitary functions, including serum prolactin (7.5 μg/L), α-subunits (3.9 μg/L), and basal growth hormone (1.5 mU/L), were normal.

The nasopharyngeal and sellar parts of the tumor were extirpated via a transseptal transsphenoidal approach. The tumor appeared to have invaded the nasopharynx through the natural ostium of the sphenoid sinus. The suprasellar component could not be reached. The tumor was found to have a firm consistency preventing descent into the vacant space at the sellar level.

Histologic examination showed a sinusoidal tumor with nuclear polymorphism and some mitotic figures. Immunohistochemical staining showed growth hormone and prolactin-containing granules, indicating a mixed type pituitary adenoma without secretory activity.

Three months after transsphenoidal surgery, removal of the suprasellar part of the tumor was attempted via a transcranial approach. However, total removal proved to be impossible, probably because of an unpredictable "prefixed" optic chiasm that restricted access to the adenoma.

Although the visual acuity and fields normalized completely, a small suprasellar tumor remnant remained visible on the CT scans, even after 6 months of bromocriptine (0.5 mg tid). Therefore, 40-Gy megavolt irradiation was given via two opposing fields for 4 weeks.

At the last follow-up, 2 years after the first opera-

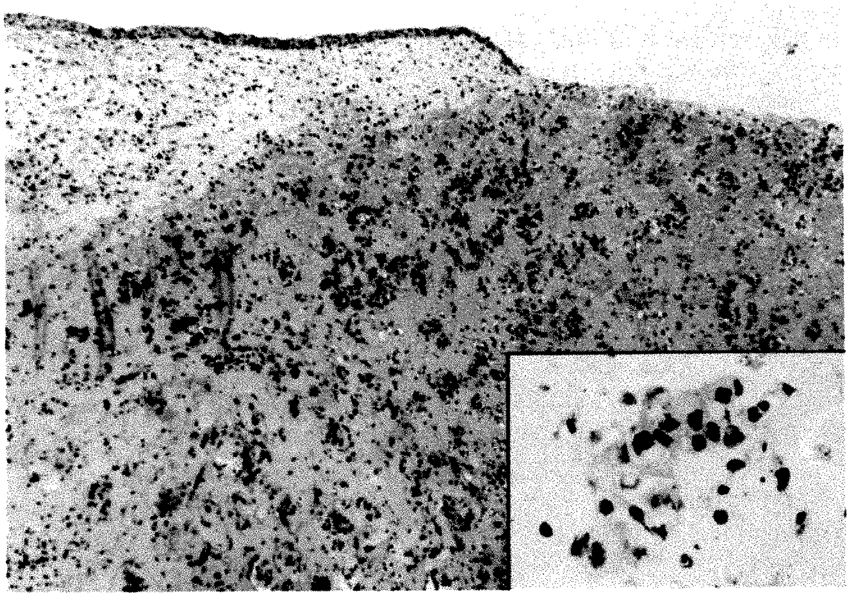

Fig 3. (Case 1) Section of nasal mucosa biopsy specimen covered with epithelium and showing subepithelial proliferation of small groups of tumor cells (H & E, original x125). Inset) Similar group of cells with fine-granular cytoplasm at higher magnification (original x350).

tion, the patient was in good condition without complaints. Computed tomographic scanning did not show measurable tumor reduction. Prior to irradiation, the patient had become dependent on endocrine substitution (hydrocortisone 40 mg and levothyroxine 0.2 mg daily).

Case 3. In 1959, a 47-year-old woman had been referred because of intermittent nosebleeds and persisting occipital headache during the last 6 months. A few weeks before admission she had complained of decreased visual acuity of the left eye and periods of diplopia. Paralysis of the left oculomotor nerve was diagnosed. Otolaryngic inspection revealed a large tumor in the nasopharynx. Partial tumor extirpation was performed via a left frontal craniotomy, combined with decompression of the left optic nerve. Histologic examination showed the tumor to be a chromophobe pituitary adenoma. Postoperatively, the patient was irradiated (details not available). During the following 13 years there were no complaints, but in 1972 she developed a frontal headache and disturbance of visual acuity of the right eye. She also complained of nasal obstruction on the left side. X-ray polytomography showed a large tumor in the left ethmoid complex and nasal cavity, with destruction of the medial bony wall of the maxillary sinus. Cerebral angiography revealed upward displacement of the communicating anterior cerebral artery, suggesting suprasellar extension. On inspection the tumor was seen near the left middle turbinate, a biopsy specimen of which also showed chromophobe adenoma cells. During a second frontal craniotomy, now on the right side, decompression of the right optic nerve was accomplished.

During the next 5 years the patient remained fair-

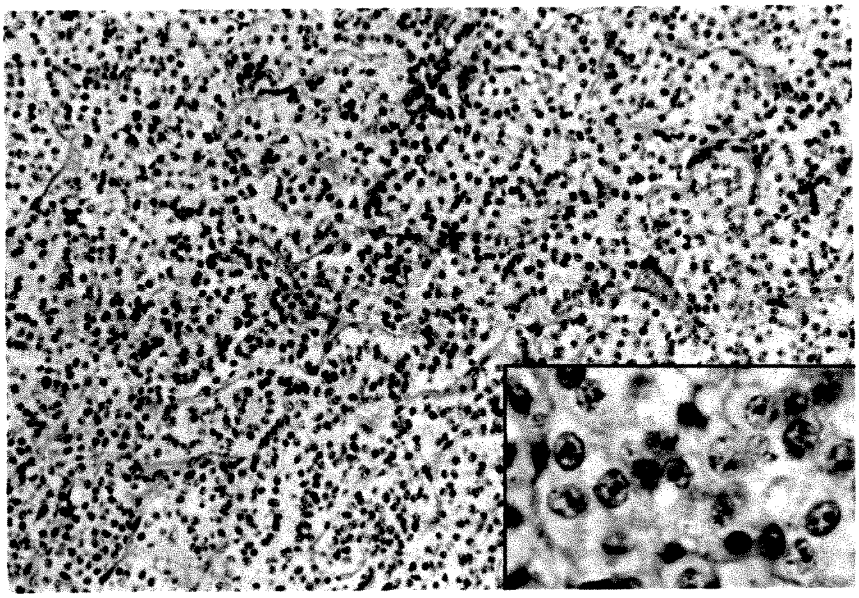

Fig 4. (Case 1) Tissue removed at surgery showing adenoma with its alveolar architecture and homogeneous cell population (H & E, original x125). Inset) Original x500.

ly well, but then once again the visual acuity of the right eye decreased. Computed tomographic scanning showed tumor extension into the left ethmoid-sphenoid complex as well as into the suprasellar and parasellar regions. In a third operation (May 1977), complete tumor extirpation was performed via a transseptal and transsphenoidal approach, and a Caldwell-Luc procedure on the left side. Histologic examination revealed a chromophobe adenoma, and immunochemistry showed no hormone-containing granules.

Postoperative endocrine studies revealed no gross abnormalities except a slightly elevated level of serum prolactin (20 μg/L). Computed tomographic scanning in 1979 revealed an empty sella without signs of extrasellar tumor remnants. The visual acuity of the right eye remained unchanged (0.6), and further follow-up after hydrocortisone supplementation was uneventful. In 1984, 7 years after the last operation, the patient died at the age of 72 in a nursing home. As far as we know, the cause of death was not related to the pituitary disorder.

DISCUSSION

Nasopharyngeal extension of a pituitary adenoma is a very uncommon tumor complication. A review of the literature indicates that its incidence has not changed in the last 45 years. We have seen three cases among our own series of 187 pituitary tumors covering a 10-year period (1976 to 1985). An incidence of 2.3% was reported in 1938 by Henderson,[2] who described eight patients in a series of 338, and in 1985 Pia et al[3] found an incidence of 2.5% (4/156 patients). In view of the rise of the known incidence of large or giant adenomas from 11% to 17.5% since the introduction of the CT scan, this observation is even more striking.

Aside from usual symptoms attributable to the tumoral mass effect, such as headache, visual field defects, loss of visual acuity, and symptoms due to pituitary failure or hypersecretion, some patients develop symptoms such as nasal obstruction, recurrent epistaxis, intermittent mucoid nasal discharge, or postnasal drip.[10-14] During otolaryngic examination, the tumor can be seen in the nasal cavity or nasopharynx, and with great care a biopsy can be performed.[15]

In 1912, Cushing[1] was the first to publish well-documented case histories on pituitary tumors with nasopharyngeal signs and insisted on including an otolaryngic examination as part of his routine workup. These three cases were reported before the introduction of radiology as an aid to the diagnosis of pituitary tumor.

Conventional radiology including plain films, tomography, cerebral angiography, and pneumoencephalography of the basal cisterns yields no more than a fragmentary picture of the pathologic sellar process.[13,15] Currently, high resolution CT is a very valuable diagnostic procedure for the evaluation of pituitary tumors, and CT scanning in two directions is the method of choice for visualization of the lesion in relation to its bony boundaries (Fig 1). Nevertheless, sometimes it is difficult to differentiate between tumor extension and opacification due to sinus obstruction. In such cases use can be made of MRI. According to its MRI characteristics, a tumor will give rise to a low signal emission in T1-weighted (Fig 2A), and an increased signal in T2-weighted images, whereas swollen mucosa and mucus will induce emission of a higher signal in the strongly T2-weighted images. In this way swollen mucosa and mucus can be differentiated from tumor tissue (Fig 2B,C).

The literature offers several speculative discussions on growth patterns of pituitary tumors. In 1940, Jefferson[16] defined six possible pathways of tumor extension, among which he considered downward growth into the sphenoid sinus to be the most common. He cited several mechanical factors with a possible role in extrasellar extension, but none of them provides a satisfactory explanation. Moreover, it is not understood why some adenomas tend to grow downward, passing beyond the bony boundaries of the sphenoid sinus into the nasal cavity. It is remarkable that in one of our cases (case 2) the tumor appeared to have used the natural ostium of the sphenoid sinus as an avenue of extension.

Recently, Scheithauer et al[17] performed an immunohistochemical and ultrastructural analysis of 365 pituitary adenomas. Based on this series, the estimated rate of gross extrasellar expansion by pituitary adenomas of all types is approximately 35%. Correlation was found between the frequency and the nature of invasiveness and the functional type of the adenoma. For example, the prolactin cell type adenoma (24 cases) and the mixed growth hormone prolactin cell type (35 cases) can expand in any direction, but the preferential pathway is infrasellar. Such tumors often invade the sphenoid bone and occasionally grow further downward to appear in the nasopharynx or nasal cavity. The adrenocorticotropic hormone–producing adenomas, for example, tend to grow upward and show suprasellar extension.

On the other hand, in their evaluation of 48 pituitary tumors with hyperadrenalism, Rovit and Berry[18] mentioned only one case with growth into the nasopharynx. So far, apart from the one patient described by Cushing,[1] acromegaly has not been found in association with such tumor extension. Lüdecke's series of 327 cases confirmed the rarity of nasal tumor localization in acromegaly (personal communication).

In our patients both infrasellar and suprasellar extension was observed. In two of them the tumor was a prolactinoma or mixed type, whereas the tumor in the third had no hormone-containing granules.

The histopathologist receiving tissue with undifferentiated tumor material from the nasal region, as in case 1, must differentiate between lymphoma, esthesioneuroblastoma, undifferentiated carcinoma, and pituitary adenoma. Especially in such cases, immunohistochemical analysis can be helpful. Lymphoma cells are stained for common leukocyte antigen, most carcinomas for cytokeratins, and esthesioneuroblastomas for neuron-specific enolase and glial fibrillary acidic protein. Pituitary adenoma is stained for neuron-specific enolase and the pituitary hormones. The importance of the histologist's contribution to the diagnostic workup is underscored by case 1. The conclusive demonstration of prolactin-containing tumor cells in a biopsy made us realize that this was a pituitary tumor and led to an early endocrine analysis.

In cases 2 and 3, the surgical material provided more and differentiated tumor tissue in which the growth pattern and cytologic detail together with the clinical indications facilitated the diagnosis greatly.

With respect to the differential diagnosis concerning an easily bleeding tumor in the nasal cavity, a large number of benign and malignant tumors can be listed, among which the most frequent and important are squamous cell carcinoma and adenocarcinoma of the paranasal sinuses and nasal cavity. However, the presence of a tumor within the nasal cavity or nasopharynx combined with evidence of a sellar process does not always indicate a downward-growing pituitary tumor. One also should consider upward extension of a nasopharyngeal carcinoma,[19] which has been seen twice in our center in recent years. Other diagnoses to be considered are juvenile nasopharyngeal angiofibroma,[20] chordoma,[21] craniopharyngioma,[22] esthesioneuroblastoma, sphenoid sinus mucocele,[23] meningioma[24] or giant cell tumor, giant aneurysm, and carcinoma of the sphenoid sinus.

From the review of the literature it is evident that complete removal of these large invasive tumors is exceptional.[3,25] Consequently, there is a growing tendency to use dopaminergic agents such as bromocriptine as primary treatment for macroprolactinomas and gonadotropin-secreting adenomas, which are often exceptionally large. Bromocriptine reduces both the secretory activity and the size of the tumor in over 50% of adenomas of these types, but usually is not effective in nonfunctioning pituitary tumors. Therefore, for bromocriptine-sensitive tumors, surgery or potentially harmful supplementary radiotherapy may no longer be required.

However, surgical treatment is obligatory when the tumor has destroyed the base of the skull, as in the patients reported here. In these cases a transseptal transsphenoidal approach is preferred to the transcranial route, which has become second-choice surgical treatment for the vast majority of pituitary tumors. Furthermore, via this route it is possible to repair the bony defect, the presence of which in the skull base carries a risk of CSF rhinorrhea and ascending infection. Cerebrospinal fluid rhinorrhea may develop as a sign of tumor regression during preoperative bromocriptine therapy.[26]

In summary, we wish to emphasize the importance of early recognition of the type of adenoma presented and the need for close cooperation between otolaryngology and other disciplines, both clinical and nonclinical, involved in the investigation and treatment of patients with sellar disorders.

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EYES OPEN VERSUS EYES CLOSED: EFFECT ON HUMAN ROTATIONAL RESPONSES

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The effect of eyelid closure on the response to rotational vestibular stimulation was assessed by evaluating 16 normal human subjects with both earth vertical axis (EVA) and earth horizontal axis (EHA) yaw rotations with either eyes closed (EC) or eyes open in the dark (EOD). Results indicated that for EVA rotation, the subjects' responses were of larger magnitude and less variable with EOD than with EC. However, for EHA rotation, responses were of larger magnitude and equally variable with EC as compared to EOD. Our data also indicated that the quality of the EHA response with EC was altered because eyelid closure influenced the amount of periodic gaze. We conclude that eyelid closure has an effect upon both canalocular and otolithocular reflexes and suggest that both EVA and EHA rotational testing be performed with EOD rather than with EC.

KEY WORDS — electro-oculography, eyelids, rotation, vestibulo-ocular response.

INTRODUCTION

The response of normal human subjects to vestibular stimulation is known to depend upon the condition of the eyelid, that is, upon whether the eyelids are closed (EC) or are open in the dark (EOD). This effect has been quantitated for caloric testing[1] wherein responses were shown to be of higher magnitude and decreased variability in the EOD versus the EC condition. The purpose of this study was to test the hypothesis that eyelid condition affects the responses to rotational vestibular stimulation.

We evaluated both earth vertical axis (EVA) and earth horizontal axis (EHA) yaw rotational responses. Our EHA rotational protocols were designed to elicit a dynamic otolithocular response by using constant velocity stimulation. We were able thereby to evaluate the effect of eyelid condition on both semicircular canalocular and otolithocular reflexes.

METHODS

Subject Population. Sixteen normal human subjects were tested. These individuals had no history of otologic or neurologic disease. In addition, their responses to ocular motor and caloric testing were within normal limits for our laboratory. The subjects ranged in age from 21 to 36, with a mean age of 26.5. There were eight women and eight men. The subjects were divided into two equal groups. One group underwent rotational testing with EC, and the other with EOD.

Stimulation Paradigms. Each subject was tested once per week for each of 6 weeks with both EVA and EHA rotation. The EVA testing consisted of sinusoidal rotation on a computerized rate-of-turn table at 0.1 Hz with a peak stimulus velocity of 50°/s. The EHA rotations were velocity trapezoids described in detail elsewhere.[2] Briefly, the subjects were rotated about their rostral-caudal axis while earth horizontal. Following 0.6 seconds of rotational acceleration at 100°/s/s, the subjects were maintained at a constant rotational velocity of 60°/s for 60 seconds and then decelerated to a stop. For each EHA test, the subjects were first rotated clockwise (CW), ie, from supine to right lateral to prone to left lateral to supine, for 60 seconds. Following an interval of about 5 minutes, the subjects were rotated counterclockwise (CCW). For each subject, EVA testing was performed before EHA testing.

Eye Movement Response. Eye movements were recorded with bitemporal electro-oculography (EOG). The EOG signal was fed to a DC coupled amplifier with a high frequency cutoff of 40 Hz. The amplified EOG signal was connected to both a chart recorder and a 12-bit analog-to-digital converter for computer disk storage and off-line analysis. The eye movement analysis has been described in detail elsewhere.[3] Briefly, the eye movement response to both EVA and EHA rotation was analyzed by an algorithm that detected fast components of vestibular induced nystagmus so that cumulative slow component eye velocity could be analyzed. For EVA rotations, slow component eye velocity was used to compute gain and phase of the vestibulo-ocular reflex. For each subject, gain and phase values were averaged across the six test sessions. Then, gain and phase values were averaged across subjects within the EC and EOD groups.

For EHA rotations, EOG data were used to compute the magnitude of the "modulation" (MOD) and the "periodic gaze" (PG) components.[2] The

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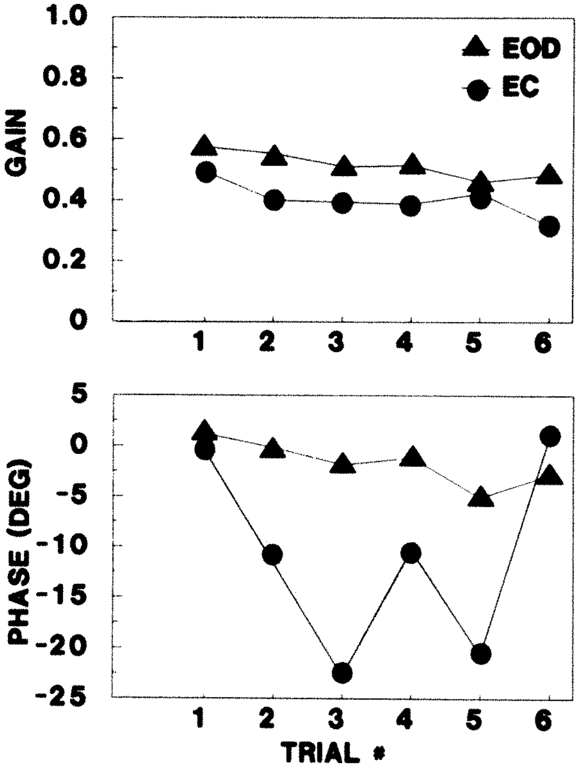

Fig 1. Gain and phase data from earth vertical axis rotation at 0.1 Hz for each of six trials. Data were averaged within groups with eyes open in dark (EOD) and with eyes closed (EC).

MOD component can be thought of as the best fit sinusoid through the processed slow component velocity data. The PG component can be thought of as the best fit sinusoid through the digitized unprocessed EOG data itself. Response amplitudes were estimated by use of discrete Fourier transforms and cross-correlation techniques. Phase represents the position of the head at which the maximum response occurs. It is measured from the nose-up position in the direction of the rotation. For example, if the response maximum occurred with the right ear down during a CW rotation, the phase lead would be 90°. For each subject, MOD and PG values were averaged for CW and CCW trials.

Our data suggested that a portion of the MOD component was a direct result of periodic changes in mean eye position (ie, the PG component). To quantitate this contribution of the PG component to the MOD component, we first mathematically differentiated the PG component, an eye position quantity, to yield PG′, an eye velocity quantity. Then, the proportion of MOD due to PG was computed as the ratio PG′/MOD, ie, the magnitude of PG′ divided by the magnitude of MOD. This ratio then was used to classify quantitatively each subject's EHA response, as will be discussed in Results.

RESULTS

Shown in Fig 1 are EVA gain and phase at 0.1 Hz versus trial number. Each data point represents gain or phase averaged across the entire EOD or EC group. It can be seen that the magnitude of EVA gain is greater in the EOD group than in the EC group for each trial. These data then were averaged across all six trials within the EOD and EC groups, and the averages are shown in the Table. It can be seen that with EOD, the gain is larger and less variable than with EC. The phase of the response is also more variable with EC than with EOD.

Figure 2 illustrates the magnitude of the EHA MOD component versus trial number for each of the 16 subjects. Note the generally larger magnitude of the MOD component in the EC group. These MOD component magnitudes and the other EHA data were averaged across all six trials and also averaged across subjects within the EOD and EC groups, and the averages are shown in the Table. It can be seen that the average magnitude of the MOD component is larger with EC than with EOD. Although the standard deviation is larger with EC, the coefficient of variation (standard deviation divided by mean value) of the response is nearly the same for EC and EOD. The magnitude of the PG component is also larger for the EC than the EOD condition. Again, although the standard deviation is larger with EC, the coefficient of variation of the response is nearly the same for EC and EOD. The phase of the MOD and PG components was not influenced significantly by eyelid closure.

Thus, our data show that for EVA rotation, a larger magnitude response is seen with EOD than with EC, and for EHA rotation, a larger magnitude response is seen with EC than with EOD. This discrepancy may be related to a qualitatively different eye movement response in the EC trials as compared to the EOD trials. Figure 3 depicts three different response types that were seen in our subject group during EHA testing. Response type 1, shown in Fig 3A, has a robust vestibular nystagmus with a clear distinction between slow and fast components, together with a small PG component. In contrast, type 3 responses, shown in Fig 3C, contain

GAIN AND PHASE VALUES FOR ROTATIONAL TESTING (MEAN ± SD)

Eye Condition	*EVA Response at 0.1 Hz*		*EHA Response at 0.16 Hz*			
			Modulation Component		*Periodic Gaze Component*	
	Gain	*Phase* (°)	*Magnitude* (°/s)	*Phase* (°)	*Magnitude* (°)	*Phase* (°)
Open in dark	0.52 ± 0.15	−1.7 ± 5.1	5.4 ± 2.1	229.98 ± 63.40	3.67 ± 3.17	338.68 ± 78.55
Closed	0.41 ± 0.19	−4.5 ± 9.2	11.2 ± 5.7	224.13 ± 51.27	12.59 ± 11.14	309.63 ± 53.50

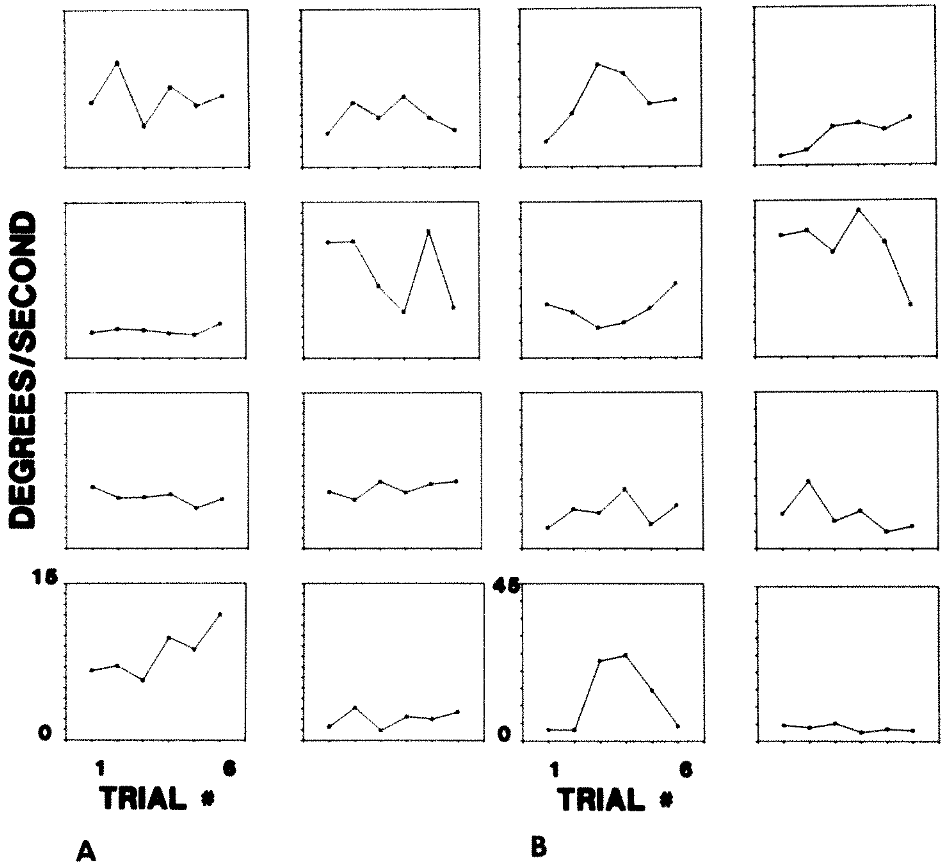

Fig 2. Earth horizontal axis rotation modulation component magnitudes for each subject for each of six trials. A) Subjects with eyes open in dark. B) Subjects with eyes closed. Note difference in ordinate scaling for two groups.

large changes in mean eye position and thus have a large PG. Definite nystagmus is lacking. Figure 3B illustrates an intermediate response, designated as type 2. Occurrences of each response type were seen in both the EC and EOD trials.

The response to each EHA trial was classified quantitatively by computing the portion of the MOD component that was due to PG′. This was accomplished by computing the ratio of the magnitude of PG′ to the magnitude of MOD. Responses in which PG′ accounted for less than 60% of MOD were classified as type 1. Responses in which PG′ accounted for greater than 90% of MOD were classified as type 3. Others were classified as type 2.

As shown in Fig 4A for CW trials, there was a preponderance of type 1 responses in the EOD subjects, and a preponderance of type 3 responses in the EC subjects. As shown in Fig 4B, the CW type 3 responses that were seen in the EC group had larger absolute PG′ values than those type 3 responses that were seen in the EOD group. This predominance of type 3 responses with large magnitude PG components in the EC group resulted in a larger average magnitude of both the MOD and the PG components for the EC as compared to the EOD condition. A similar result was found for CCW trials.

In summary, the results show that eyelid closure influences both vertical axis and horizontal axis rotational responses, but in fundamentally different ways.

DISCUSSION

Our data indicate that the response to EVA rotational testing is affected by eyelid closure in a way comparable to its effect on caloric vestibular stimulation,[1] ie, slow component eye velocity magnitude is increased and response variability is decreased with EOD as compared to EC. However, our data indicate that the eye movement response to EHA rotational vestibular stimulation is larger with EC than with EOD. Further, the larger magnitude of response with EC as compared to EOD during EHA rotation is primarily the result of large periodic changes in mean eye position.

As mentioned previously by Wall and Black,[2] the MOD and PG components of the response to EHA rotation are correlated. The large increase of both the MOD and the PG components in the EC as compared to the EOD conditions suggests that the mathematic derivative of the PG component, PG′, may have a causal influence upon the computation of the MOD component.

The smaller periodic changes in mean eye position and thus smaller PG components in the EOD trials may be related to an effect on gaze position engendered by an intent to look straight ahead. Barnes[4] has shown quantitatively that visual fixa-

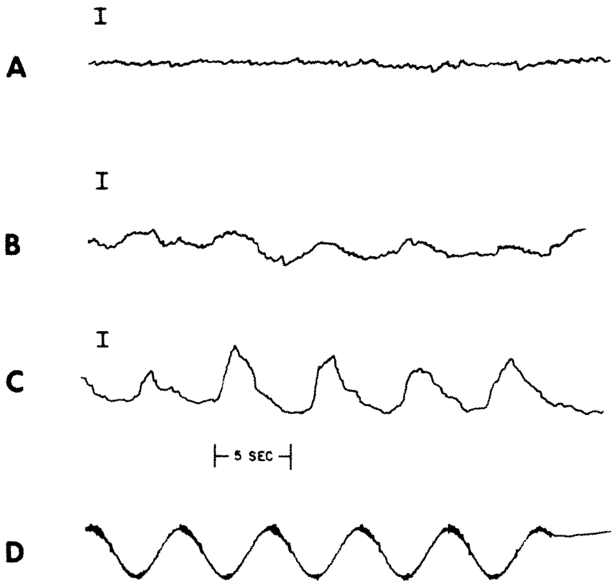

Fig 3. Examples of three types of response to earth horizontal axis rotation. A) Type 1 response, in which there is very small modulation of mean eye position. B) Type 2 response, in which modulation of mean eye position is of intermediate magnitude. C) Type 3 response, in which there is large modulation of mean eye position, and thus large periodic gaze component. Each trace represents horizontal eye position as recorded with bitemporal electro-oculography. Calibration marks indicate 20° of horizontal gaze deviation. D) Orientation of subject during stimulus. Maxima indicate nose up and minima indicate nose down.

tion during rotational induced eye movements reduces the modulation of mean eye position. Also, in patients with deficits in ocular pursuit, the eye movement response to rotation while attempting to fixate a discrete target reveals a dramatic effect on mean eye position with a much smaller effect on the slow component eye velocity of vestibular nystagmus.[5,6] Thus, the EOD condition may have induced an intent to fixate, thereby markedly reducing changes in mean eye position, and thus reducing the magnitude of the PG component.

Arousal, which may be affected by eyelid closure, is known to influence vestibular nystagmus. A low level of alertness causes a lack of robust postrotatory nystagmus[7] and also is associated with large changes in mean eye position during EVA rotation.[8] Thus, the large changes in mean eye position seen in the EC trials may have been caused by a low level of alertness during testing. However, EHA rotation is a novel stimulus that lasts for only 60 seconds per trial, making a reduced level of arousal unlikely.

Eyelid closure is known to influence other types of nystagmus, namely, congenital nystagmus and the nystagmus caused by certain brain stem lesions. Congenital nystagmus, which is typically present with fixation, is markedly diminished with EC.[9] Also, with EOD, congenital nystagmus may still be present,[10] suggesting that is is the intent to view rather than the actual visual stimulation that influences the nystagmus. In certain brain stem lesions, caloric nystagmus becomes much more prominent with fixation than without fixation,[11] a paradoxical effect.

We suggest that rotational vestibular testing using both EVA and EHA rotation should be performed with EOD rather than EC. Our conclusion is based upon the fact that the response to EVA testing is of larger magnitude and lower variability with EOD. For EHA testing, EOD leads to a response that is more likely to have a robust nystagmus with a minimum of modulation in mean eye position. Using EOG, which has a limited range of linearity, EOD testing allows a more accurate estimate of the slow component eye velocity of vestibular nystagmus.

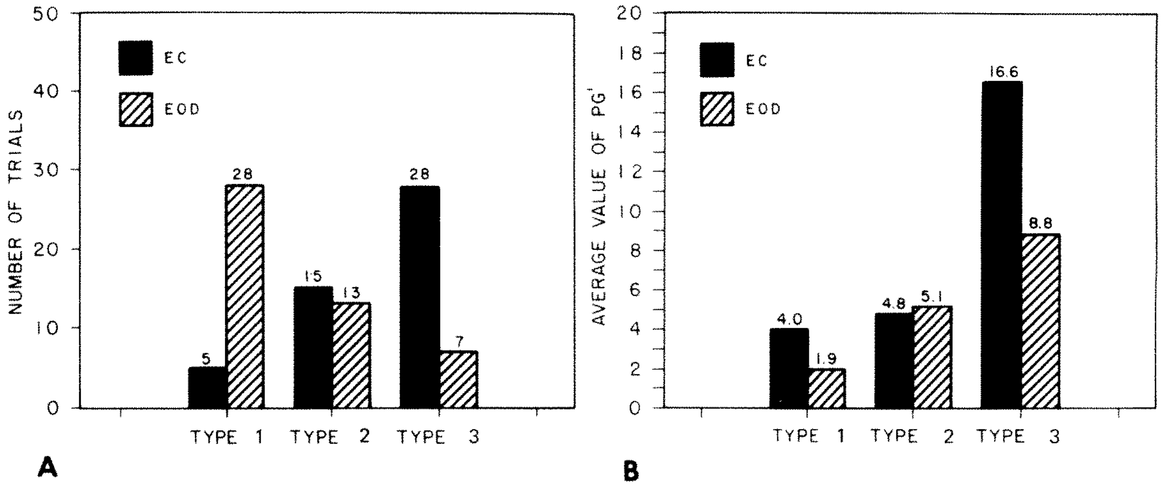

Fig 4. A) Bar graph of number of clockwise earth horizontal axis trials that could be characterized as types 1, 2, or 3, for eyes closed (EC) and eyes open in dark (EOD). Responses were classified on basis of percentage contribution of derivative of periodic gaze component to modulation component (see text). B) Bar graph showing average magnitude of derivative of periodic gaze component (PG′) for clockwise response types 1, 2, and 3.

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EUSTACHIAN TUBE LUMEN: COMPARISON BETWEEN NORMAL AND INFLAMED SPECIMENS

JACOB SADÉ, MD MICHAL LUNTZ, MD

KFAR SABA, ISRAEL

This study presents measurements of the cross-sectional luminal area of the eustachian tube. Comparisons are made between the lumens of eustachian tubes obtained from temporal bones presenting acute or secretory otitis media and those from noninflamed temporal bones. The material consisted of 71 temporal bones obtained postmortem from individuals up to 2 years of age. Forty-six of these showed no middle ear inflammation, while 25 presented either acute or secretory otitis media. In both groups the lumens of all the eustachian tubes were patent, presenting no obstruction. The mean cross-sectional area of the lumens of inflamed temporal bones was smaller than that of the noninflamed ones. This difference was not found to be statistically significant in the cartilaginous regions and was found to be statistically significant or borderline significant in the bony parts of the eustachian tube.

KEY WORDS — eustachian tube, otitis media.

INTRODUCTION

Acute and secretory otitis media (AOM, SOM) are widely thought to follow in the wake of an inflammatory obstruction or a narrowing of the eustachian tube (ET), both of which are believed to lead to inadequate aeration of the middle ear (ME).[1-4]

In our previous studies in which we compared the ET lumens of 42 infants with healthy temporal bones (TBs) with those of 19 infants whose TBs were harboring AOM or SOM, all the lumens were found to be patent.[5-13] Furthermore, although the cross-sectional areas of the lumens in the diseased TBs were smaller than those in the healthy ones, especially in the segments adjacent to the ME,[13] the average cross-sectional area of the ET lumen in its various segments did not differ significantly between the two groups.

In another study using the same material,[14] a small degree of persistent inflammatory involvement of the ET mucosa was observed in TBs with AOM or SOM. Such involvement, even though slight and confined mainly to the wide pretympanic region, nevertheless seemed to demand that we review and clarify our previous finding that did not show a significant difference between the average cross-sectional luminal areas of inflamed and noninflamed ETs. This was the purpose of the present study.

METHODS AND MATERIAL

Seventy-one TBs were fixed and decalcified in 3% nitric acid. At various stages of decalcification the TBs were trimmed and cut into four small blocks, one containing the ME and three containing parts of the ET in consecutive order. When decalcification was completed, the blocks were rinsed with water and immersed in 20% sodium sulfate solution to neutralize and remove excessive acid. Dehydration was carried out with increasing concentrations of ethanol, and thereafter the blocks were embedded in paraffin, care being taken that the plane of microtome sectioning thereafter was perpendicular to the long axis of the ET.

The blocks were sectioned serially, the thickness of the sections being 10 μm. Staining was performed with hematoxylin and eosin, PAS, and Masson trichrome.

Since the ET is not uniform in structure throughout its length, it was divided into six topographic segments[15] for purposes of comparison between corresponding regions (Fig 1).

1. *Pharyngeal Portion.* This is the anteromedial portion of the tube. In the postmortem specimen it has a curved, slitlike lumen. Glands are present in the subepithelial connective tissue on both sides of the lumen. The levator and tensor palatini muscles are well developed.
2. *Midportion.* This region resembles the previous one except that glands are found only on the medial aspect of the lumen; on its lateral aspect they are replaced by a fat pad.
3. *Near-Isthmus.* In this segment the lumen is almond-shaped and shorter. The medial cartilaginous segment is smaller, glands have disappeared, and only a few fibers of the tensor and levator palatini muscles are present.
4. *Isthmus.* The isthmus, ie, the narrowest rigid part of the ET, was found not to be a point but to extend for several millimeters. The lumen is oval and is surrounded by rigid tissue consisting of the tubal cartilage at its superior aspect and the petrous temporal bone around all the rest. The tubal muscles no longer are visible and the tensor tympani muscle now can be seen above the lumen. The caplike tubal cartilage interposes between the lumen and the tensor tympani muscle.
5. *Post-Isthmus.* In this segment the lumen cross

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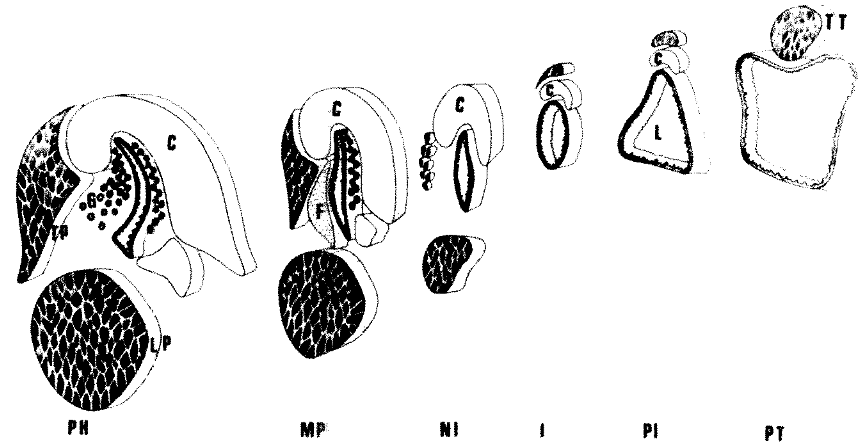

Fig 1. Schematic illustration of segments of eustachian tube: pharyngeal portion (PH), midportion (MP), near-isthmus (NI), isthmus (I), post-isthmus (PI), and pretympanum (PT). C — cartilage, TP — tensor palatini muscle, G — glands, LP — levator palatini muscle, F — fat pad, L — lumen, TT — tensor tympani muscle.

section is roughly triangular in shape and is considerably wider than that in the isthmus. The tensor tympani muscle is clearly visible at the superior aspect of the lumen, and in most cases a small cap of cartilage still can be seen below it.

6. *Pretympanum.* This last segment of the tube joins with the tympanic cavity. The lumen is roughly quadrangular and much larger than in any of the previous segments. The tensor tympani is prominent and bulges into the lumen to form its typical convex roof. The internal carotid artery lies medial, very close to the lumen, and the anterior portion of the cochlea is visible at the posteromedial aspect of the lumen.

The studied material consisted of 71 TBs removed postmortem from children ranging from 1 to 24 months of age. Because each of the 71 TBs was divided into four blocks, several sections at the beginning or the end of each block were imperfect or lost. We were forced to reduce the number of each of the six available ET regions to 52 pharyngeal, 61 midportion, 57 near-isthmus, 60 isthmus, 52 post-isthmus, and 51 pretympanum. These were considered to represent each of the six regions in a perfect manner, and only these were measured and evaluated statistically.

Forty-six of the bones exhibited no ME disease and therefore were considered as normal. Of the remaining 25 TBs, 15 showed histologic changes of the ME compatible with AOM, and ten, with SOM. Acute otitis media was characterized by the presence of an inflammatory exudate in the ME cavity, an intact drum, and an inflammatory infiltration of the mucosa, while SOM was defined by mucus in the ME cavity, an intact drum, the presence of glands in the submucosa, and areas of secreting epithelial cells.[16] The age distributions of the normal and diseased specimens as analyzed by Student's t test were similar (Tables 1 and 2).

TABLE 1. AGE DISTRIBUTION OF NORMAL AND DISEASED TEMPORAL BONES

Age (mo)	*No. of Normal Temporal Bones*	*No. of Diseased Temporal Bones*
1	9	6
2	3	1
3	1	0
4	1	0
5	2	3
6	7	5
7	5	2
8	7	0
9	1	0
12	0	4
18	3	1
24	7	3
Total	46	25

The luminal cross-sectional area of each of the above segments was measured with the aid of a light microscope fitted with a viewer on which a special grid was mounted. This apparatus made it possible to measure within an accuracy of 0.01 mm.[5-13] Differences between the measured luminal cross-sectional areas of normal and diseased TBs were assessed statistically by means of Student's t test.

RESULTS

Examination of all 25 specimens showing evidence of AOM or SOM verified our previous finding[5-13] that the ET was patent throughout its length in each case.

The lumens from different individuals showed considerable variations in size, consistent with normal biologic distribution. The patterns of size distribution in the inflamed and noninflamed groups were similar (Fig 2).

The mean values of the cross-sectional areas of the different ET segments are recorded in Table 3.

TABLE 2. MEAN VALUES OF AGE FOR NORMAL AND DISEASED TEMPORAL BONES

	Normal	*Diseased*
Mean age (mo)*	8.609	8.200
Standard deviation	7.770	7.388
Maximal age (mo)	24	24
Minimal age (mo)	1	1

*p = .8302.

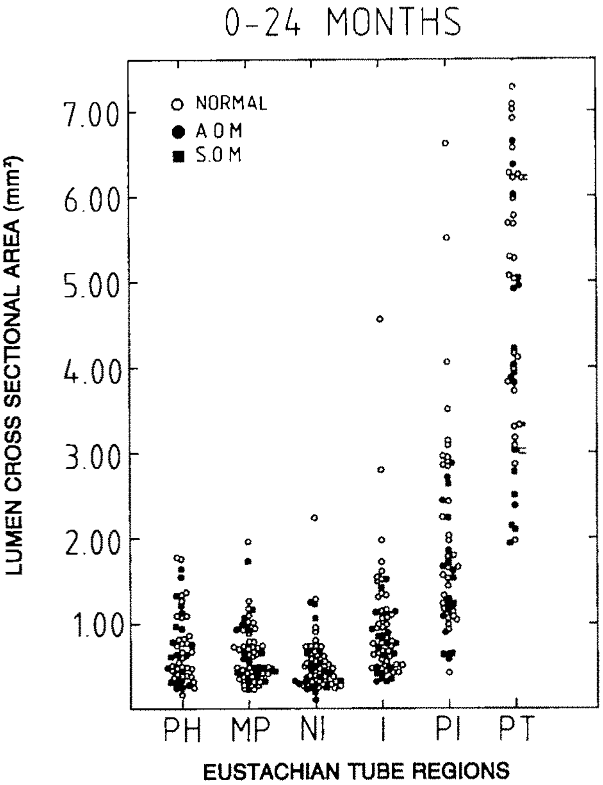

Fig 2. Distribution of eustachian tube lumen size of all specimens examined. Abbreviations as in Fig 1. For PT, four exceptionally large measurements are not depicted: 9.73 mm², 8.92 mm², 8.33 mm², and 8.23 mm².

It can be seen that the mean differences between the segmental cross sections of normal and inflamed TBs increases monotonically (in absolute values) from the midportion to the pretympanic region. In the bony segments (isthmus, post-isthmus, pretympanum), these differences are on the order of magnitude of 22% to 27% (Table 3). Statistically, these differences are either borderline significant or significant. The p values obtained by Student's *t* test were .053, .087, and .030, respectively. In the three medial segments of the ET, ie, pharyngeal portion, midportion, and near-isthmus, the difference between the cross-sectional areas of the ET lumen of normal and inflamed TBs was not significant.

DISCUSSION

The pathogenesis of both AOM and SOM frequently has been attributed to a primary obstruction or narrowing of the ET, presumably resulting in inadequate aeration of the ME.[1-4] This was thought to lead in turn to an effusion within the tympanic cavity and to its defective clearance. However, our previous histologic studies[5-13] as well as the present one have shown the ET to be morphologically patent in both AOM and SOM. Furthermore, an earlier study[17] demonstrated the fact, now well known clinically, that once ventilating tubes are inserted into the eardrums of patients with SOM, the MEs clear within a few days; this indicates that the ETs of these ears are open functionally as well, as far as mucus clearance is concerned.[17] Radiopaque studies by Bluestone et al[18] also present patency of the tube in cases of SOM.

Although obstruction of the ET appears to have been ruled out by the above findings, it is nevertheless possible that narrowness of its lumen in SOM or AOM may account for aeration deficiency in these ears.

In our previous studies,[12,13] although the average cross-sectional area of the lumen in ETs from TBs showing evidence of AOM or SOM was smaller than in healthy ETs, the difference between the two groups was not significant. In another study using the same material,[14] the diseased TBs exhibited inflammatory reaction of the mucosa. Figure 3[14] summarizes this study. In Fig 3 it is seen that this reaction was very slight in the cartilaginous segment of the ET (pharyngeal portion, midportion, and near-isthmus) and showed a tendency to increase as the tube was followed backward toward the ME, becoming more pronounced in the wide pretympanic region and especially marked in the ME itself. The thickness of the mucosa of the pharyngeal portion has been taken as 1.0,[14] and the thickness of the mucosa of the rest of the segments has been calculated proportional to it, the mucosa of the mid-

TABLE 3. CROSS-SECTIONAL AREA OF EUSTACHIAN TUBE LUMENS

	Mean ± SD Luminal Cross-Sectional Area in mm²		*Mean Differences Between Normal and Diseased Specimens*		
Segment	*Normal Specimens*	*Diseased Specimens*	*mm²*	*%*	*p*
Pharyngeal portion	0.72 ± 0.41 (n = 32)	0.73 ± 0.43 (n = 20)	−0.01	− 1.3	.915
Midportion	0.65 ± 0.34 (n = 40)	0.64 ± 0.36 (n = 21)	0.01	1.5	.849
Near-isthmus	0.52 ± 0.23 (n = 34)	0.47 ± 0.30 (n = 23)	0.05	9.6	.489
Isthmus	0.96 ± 0.50 (n = 39)	0.72 ± 0.34 (n = 21)	0.24	25.0	.053
Post-isthmus	2.15 ± 1.38 (n = 32)	1.56 ± 0.77 (n = 20)	0.59	27.4	.087
Pretympanum	5.33 ± 1.88 (n = 32)	4.14 ± 1.77 (n = 19)	1.19	22.3	.030

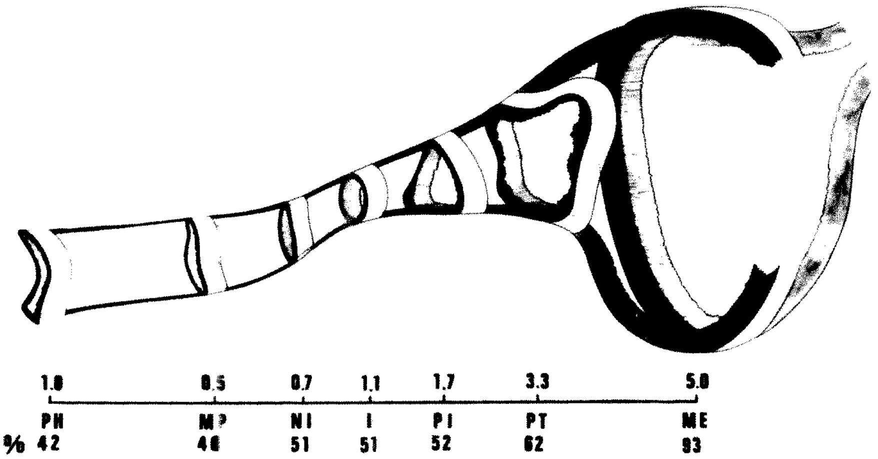

Fig 3. Distribution of relative amount of inflammatory reaction (black areas) through various eustachian tube segments. Based on data from Berger et al.[14] Abbreviations as in Fig 1. Note that inflammatory reaction increases progressively "backward," reaching peak in middle ear. Thickness of mucosa of PH has been taken as 1.0, and thickness of mucosa of rest of segments is calculated proportional to this. Percentages are of luminal circumference occupied by inflammatory reaction in each segment.

portion being 0.5, that of the near-isthmus 0.7, the isthmus 1.1, the post-isthmus 1.7, the pretympanum 3.3, and the middle ear cavity five times that of the pharyngeal portion. The percentage of the luminal circumference occupied by the inflammatory reaction in each segment varied from one region to another, showing also an increased involvement from the cartilaginous part backward as the tube reached the ME. In the pharyngeal portion 42% of the circumference presented an inflammatory reaction, in the midportion 40%, in the near-isthmus 51%, in the isthmus 51%, in the post-isthmus 52%, and in the pretympanum 62%. In the middle ear 93% of the mucosal circumference was involved in the inflammatory reaction.

TABLE 4. CROSS-SECTIONAL AREA OF EUSTACHIAN TUBE LUMENS OBTAINED IN PREVIOUS STUDY

	Mean ± SD Luminal Cross-Sectional Area in mm²		
Segment	*Normal Specimens*	*Diseased Specimens*	*p*
Pharyngeal portion	0.72±0.43 (n = 29)	0.70±0.46 (n = 14)	.912
Midportion	0.66±0.35 (n = 37)	0.64±0.39 (n = 15)	.889
Near-isthmus	0.60±0.41 (n = 31)	0.49±0.33 (n = 17)	.349
Isthmus	1.06±0.78 (n = 36)	0.73±0.37 (n = 15)	.124
Post-isthmus	2.19±1.42 (n = 29)	1.57±0.80 (n = 15)	.123
Pretympanum	5.33±1.97 (n = 28)	4.48±1.94 (n = 13)	.205

Data from Sadé et al.[13]

The present study represents an attempt to reconcile the apparently conflicting data relating to the persistent involvement of the ET mucosa on the one hand, and the statistically insignificant difference in luminal cross section between the normal and the inflamed TBs[13] on the other. More specifically, we were interested in determining whether the use of larger amounts of study material might augment the level of significance of the results. Indeed, once a larger group of TBs was studied, a statistical difference between the widths of the largest segment (the pretympanum) was revealed, although the measurements themselves did not change substantially (Tables 3 and 4[13]). The post-isthmus and the isthmus showed borderline significance (Table 3). The consistency of this pattern suggests that for practical purposes the "borderline significant" values probably also should be regarded as significant.

The finding of the present study is in line with the findings of our previous study[14] showing that both in AOM and in SOM the inflammatory reaction of the ME mucosa exceeds that found in the ET by several orders of magnitude. Moreover, the inflammatory reaction diminishes gradually along the length of the ET from the ME toward its pharyngeal portion.[14]

We would interpret these results to mean that the inflammatory reaction seen histologically in the ET is probably secondary to events in the ME. It is difficult to deduce from these findings what role the inflammatory reaction plays in airflow into the ME, mainly because very little is known yet about airflow through the noninflamed ET.

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CYTOKERATIN PATTERNS OF TISSUES RELATED TO CHOLESTEATOMA PATHOGENESIS

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Specimens of cholesteatoma matrix, meatal epidermis, and middle ear epithelium were removed during surgery, and immunohistochemical techniques were used to investigate cytokeratin expression. The use of five chain-specific anticytokeratin monoclonal antibodies and one broad specific anticytokeratin monoclonal antibody showed the divergent behavior of middle ear epithelium compared with the cytokeratin expression of the other two types of epithelium. Middle ear epithelium was characterized by the presence of cytokeratins 4, 8, 18, and 19, whereas in both cholesteatoma and meatal epidermis cytokeratin 10 predominated. Furthermore, cholesteatoma showed an infrequent focal presence of cytokeratins 4, 18, and 19. The similarity between cholesteatoma and meatal epidermis with respect to morphology, and the presence of cytokeratin 10 support an epidermal origin of cholesteatoma. However, a metaplastic origin cannot be excluded, because of the infrequent occurrence of a small amount of cytokeratins 4, 18, and 19 in cholesteatoma matrix that was not found in meatal epidermis but was a component of the cytokeratin pattern of middle ear epithelium.

KEY WORDS — cytokeratin pattern, meatal epidermis, middle ear epithelium.

INTRODUCTION

The origin of cholesteatoma is still unknown. At present, three fundamentally different theories on the pathogenesis of this cornifying epithelium in the middle ear cavity are current, one concerning a congenital origin, one of an epidermal origin, and the third postulating a metaplasia of the middle ear epithelium.

The congenital origin[1] seems to apply to only a small proportion of the total number of cholesteatomas. Many authors consider the epidermal origin as the most likely for cholesteatoma, but opinions differ on the exact mechanism by which the epidermis of either the meatal wall or the tympanic membrane invades the middle ear cavity.[2-6] The metaplasia theory[7,8] is supported by those who hold the view that certain stimuli to the middle ear epithelium lead to the development of cholesteatoma.

All tissues of epithelial origin are characterized by the presence of cytokeratin. Cytokeratins belong to the intermediate filaments and comprise a family of at least 19 polypeptides with different molecular weights (40 to 68 kd) and isoelectric pH values (pH 5.2 to 7.8).[9,10] Since each type of epithelium expresses a characteristic set of cytokeratins,[10] which according to the current literature are affected only mildly, if at all, by neoplasia and metastasis,[11] it was thought that comparison of the cytokeratin patterns of cholesteatoma, meatal epidermis, and middle ear epithelium might shed some new light on the pathogenesis of cholesteatoma.

In the present study the cytokeratin pattern of these three tissues was investigated with five chain-specific monoclonal anticytokeratin antibodies directed against cytokeratins 4, 8, 10, 18, and 19. In addition, a monoclonal antibody recognizing most cytokeratins was applied.

MATERIALS AND METHODS

Specimens were obtained from patients requiring middle ear surgery. Seven cholesteatoma, five auditory canal wall epithelium, and five middle ear mucosa specimens were analyzed with respect to cytokeratin expression. For each of these three categories, one specimen from each patient was evaluated. The specimens were placed immediately in phosphate-buffered physiologic saline (pH 7.4) at 4°C and processed within 2 hours after the operation.

Routine Transmission Electron Microscopy. Specimens were fixed in a 1.5% glutaraldehyde solution in sodium cacodylate buffer (0.14 *M*, pH 7.4, 4°C) for 2 hours, rinsed, and postfixed in 1% osmium tetroxide for 30 minutes at room temperature. Embedding techniques and ultrathin sections were essentially the same as described elsewhere.[12]

Immunohistochemistry. Material was embedded in Tissue-Tek OCT compound, frozen in liquid nitrogen, and stored at −70°C. Cryosections were cut 6 μm thick in cryostat and attached to albumin/glycerin-coated object glasses. The object glasses were kept at −20°C and processed for immunohis-

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From the Departments of Otorhinolaryngology (van Blitterswijk, Grote, Lutgert, Hesseling), Dermatology (Out), and Pathology (van Muijen), Leiden University Hospital, and the Laboratory for Electron Microscopy (Fransen), University of Leiden, the Netherlands. This study was partially supported by the Heinsius Houbolt Foundation.

REPRINTS — C. A. van Blitterswijk, PhD, Dept of Otorhinolaryngology, University Hospital, Rijnsburgerweg 10, 2333 AA Leiden, the Netherlands.

TABLE 1. CYTOKERATINS AND CORRESPONDING CHAIN-SPECIFIC MONOCLONAL ANTIBODIES

Cytokeratin	*Monoclonal Antibody*
Cytokeratin 4	6B10
Cytokeratin 8	M20
Cytokeratin 10	RKSE 60
Cytokeratin 18	M9
Cytokeratin 19	LP2K
Broad specific	C80

tochemistry within 24 hours. Before the immunostaining procedure the material on the object glasses was thawed for 1 hour at room temperature and fixed in acetone for 10 minutes. Cryosections were incubated in the presence of the anticytokeratin antibody before incubation in a rabbit anti mouse IgG/peroxidase complex. The complex was incubated with 20% pooled human serum to reduce aspecific staining. Antibodies were visualized by immersion in a 3,3-diaminobenzidinetetrahydrochloride solution containing hydrogen peroxide. For the controls the first incubation step was omitted. After the immunostaining the sections were stained in hematoxylin for 30 seconds, dehydrated in a graded alcohol series, and embedded in DPX mountant.

Transmission Electron Microscopic Immunocytochemistry. Some of the specimens were fixed for 2 hours in a phosphate-buffered (pH 7.4, 4°C) 1% formaldehyde solution to which 0.1% glutaraldehyde had been added. This was followed by fixation and storage in a similar solution, but without glutaraldehyde. Shortly before cryosectioning, the specimens were impregnated with a 2.3 *M* sucrose solution for 30 minutes and then frozen in liquid nitrogen. Ultrathin cryosections were cut at −90°C in a Sorvall MT 2B ultramicrotome with a cryoattachment. These cryosections then were incubated with the broad specific anticytokeratin antibody (clone 80) followed by incubation with rabbit anti mouse IgG and protein A gold (10 nm). Finally, the cryosections were stained and embedded in 0.3% uranyl acetate with 2% methyl cellulose. These procedures were performed according to Fransen et al.[13]

Monoclonal Anticytokeratin Antibodies. These antibodies were used as shown in Table 1. Monoclonal antibodies M9 and clone 80 were obtained from Sanbio BV (Uden, the Netherlands), RKSE 60 was from Eurodiagnostics (Apeldoorn, the Netherlands), and LP2K was provided by Dr E. Lane, London. The specificity of the antibodies has been reported elsewhere.[14-18]

RESULTS

Morphology. The morphology of cholesteatoma

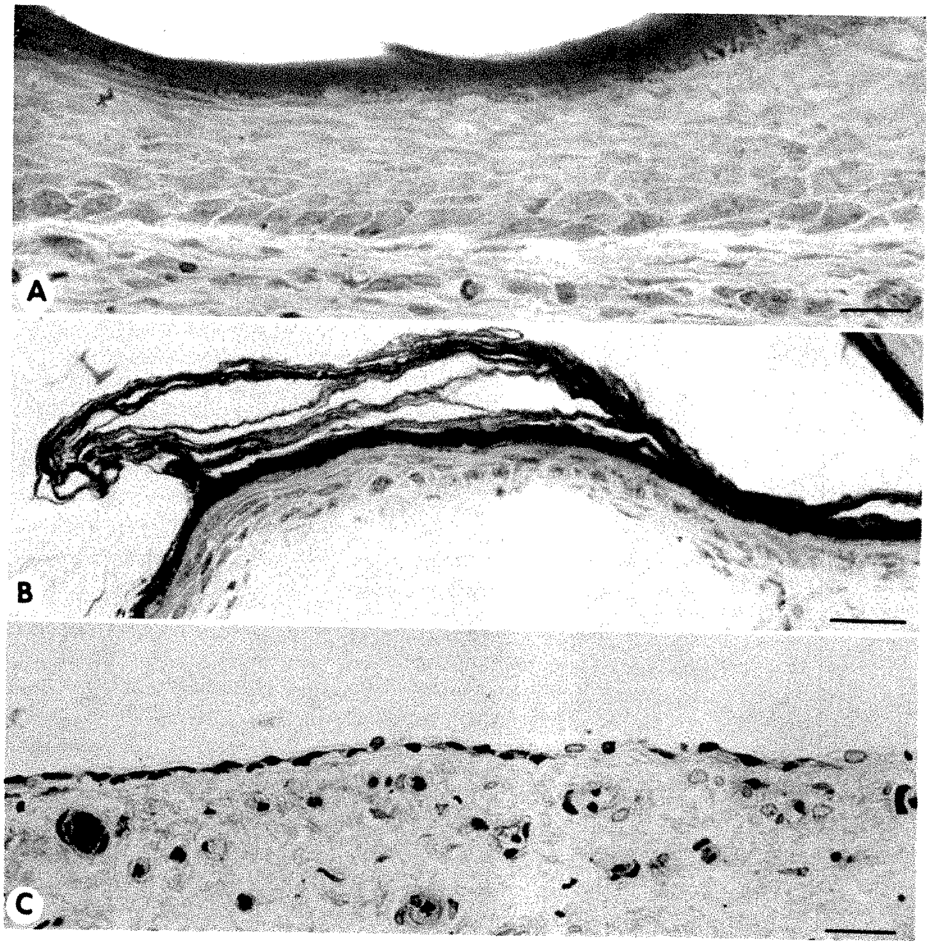

Fig 1. Light micrographs showing morphology of A) cholesteatoma matrix, B) meatal epidermis, and C) middle ear epithelium. Bars — 8 μm.

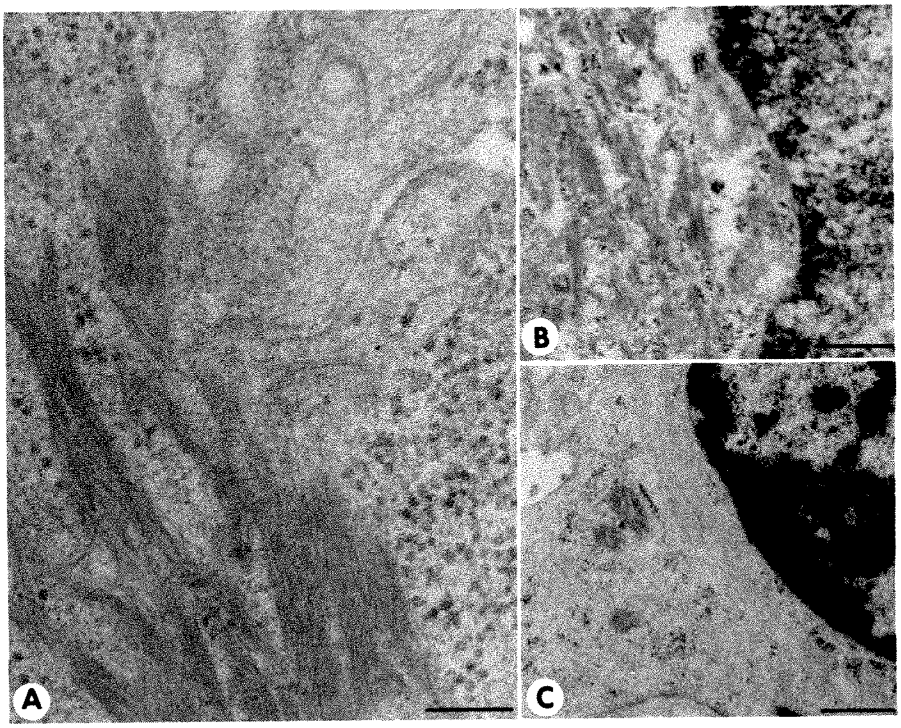

Fig 2. Transmission electron micrographs showing intermediate-like filaments in A) cholesteatoma matrix (bar — 0.2 μm), B) meatal epidermis (bar — 0.5 μm), and C) middle ear epithelium (bar — 0.5 μm).

matrix, meatal epidermis, and middle ear epithelium was studied by light microscopy and transmission electron microscopy.

Cholesteatoma matrix showed the characteristic four layers of a cornifying epithelium, ie, the stratum basale, stratum spinosum, stratum granulosum, and stratum corneum (Fig 1A). The overall thickness of the matrix without the stratum corneum ranged between two and 20 cells, the average being eight cells.

Meatal epidermis, too, showed the stratum basale, stratum spinosum, stratum granulosum, and stratum corneum (Fig 1B). Thickness without the stratum corneum ranged between eight and 20 cells (average, 13). In addition to the four strata, hair cell follicles and secretory glands sometimes were seen.

Middle ear epithelium was composed of a noncornifying epithelium generally one to two cells thick (Fig 1C). In one specimen a stratified epithelium was found (seven cell layers). All cells were flat and polygonal.

Cytokeratin Demonstration. Routine transmission electron microscopy revealed the presence of intermediate-like filaments in all three tissues studied (Fig 2). In cholesteatoma and meatal tissues these filaments were most prominent, occupying a large proportion of the cytoplasmic area. Similar filaments rarely were seen in middle ear epithelium.

Ultrathin cryosections of cholesteatoma incubated with monoclonal antibody clone 80, which has broad specificity against cytokeratin, showed positive staining of these filaments, indicating the presence of cytokeratin (Fig 3). In the immunohistochemical studies, all investigated tissues showed positive staining after incubation with clone 80. Divergence of staining characteristics was found with the other monoclonal antibodies. The exact distribution of these antibodies in the different types of tissue is given in Table 2. Control studies did not reveal any noteworthy aspecific staining.

Cholesteatoma matrix in general did not react positively with monoclonal antibodies 6B10, M20, M9, or LP2K (specific for cytokeratins 4, 8, 18, and 19, respectively). In two of seven cholesteatomas, however, a minor focal presence of cytokeratins 4, 18, and 19 was seen in the cholesteatoma matrix (Fig 4A). Cytokeratin 10 occurred in all cholesteatomas; it was seen in the stratum spinosum, stratum granulosum, and stratum corneum, but not in the stratum basale (Fig 4B).

Meatal epidermis also showed a positive reaction product with RKSE 60 in all strata except the stratum basale (Fig 5). In contrast to the cholesteatoma tissue, no foci of cytokeratins 4, 18, and 19 were observed.

Middle ear epithelium, unlike cholesteatoma and meatal epidermis, did not show a positive staining for cytokeratin 10. A positive reaction product was found in all epithelial cells for cytokeratins 4, 8, 18, and 19 (Fig 6). The specimen with a stratified epithelium comprising approximately seven cell layers showed the same staining behavior as the other middle ear epithelium specimens.

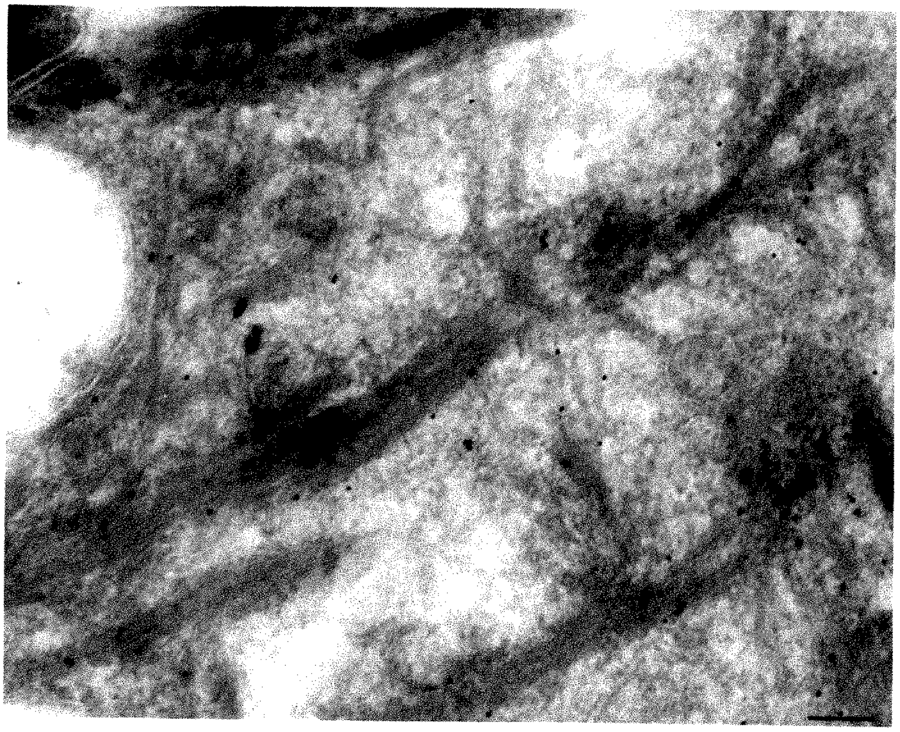

Fig 3. Transmission electron micrograph of cholesteatoma cryosection. Electron-dense gold particles indicate presence of monoclonal antibody clone 80 in intermediate-like filaments. Bar — 0.2 μm.

DISCUSSION

Several hypotheses have been proposed to explain the pathogenesis of cholesteatoma. When these hypotheses are subdivided on the basis of the epithelium giving rise to the cholesteatoma, a distinction can be made between theories postulating a congenital,[1] epidermal,[2-6] or middle ear epithelium origin.[7,8]

The morphologic similarity between cholesteatoma epidermis and the epidermis of the auditory canal wall shown by this and other studies,[19,20] both being stratified cornifying epithelia in contrast to the noncornifying middle ear epithelium, suggests an epidermal origin of cholesteatoma. However, according to Sadé et al,[7,8] metaplasia of middle ear epithelium would cause this epithelium to become a stratified cornifying epidermis that could form the basis of cholesteatoma. While this hypothesis seems to be partially supported by experiments in which middle ear epithelium showed terminal differentiation in culture,[21] it has been rejected by Palva et al,[22] who claim that the occurrence of metaplastic middle ear epithelium is limited to the advancing front of cholesteatoma and does not play a major role in the genesis of cholesteatoma.

Since each type of epithelium is characterized by a specific set of cytokeratins[10] and the overall type of cytokeratin expression is not altered after transformation,[11] it may be assumed that the tissue along the area of origin of cholesteatoma will be characterized by a cytokeratin expression similar to that of cholesteatoma. On these grounds it seemed possible that analysis of the cytokeratin pattern of cholesteatoma epidermis, meatal epidermis, and middle ear epithelium would shed some light on the controversy between adherents of the epidermis theory and the metaplasia theory.

The presence of cytokeratin in cholesteatoma and middle ear epithelium has been reported by several authors.[8,21-25] Only Palva et al[22] observed a difference in cytokeratin pattern between these two types of epithelium, but since these authors used only a polyclonal and one monoclonal antibody, this difference might reflect a single deviating cytokeratin and therefore would not exclude completely the role of middle ear epithelium in the pathogenesis of cholesteatoma.

An effort to determine the cytokeratin pattern of cholesteatoma in relation to human epidermis was made by Gillis et al,[24] who described a less complicated cytokeratin pattern for cholesteatoma on the basis of one-dimensional gel electrophoresis. Unfortunately, the human epidermis used as reference was not meatal epidermis, hence their findings are difficult to interpret in relation to the pathogenesis of cholesteatoma.

TABLE 2. STAINING CHARACTERISTICS OF FIVE CHAIN-SPECIFIC ANTICYTOKERATIN MONOCLONAL ANTIBODIES

Epithelia	*6B10*	*M20*	*RKSE 60*	*M9*	*LP2K*	*C80*
Cholesteatoma	F	–	+	F	F	+
Meatus	–	–	+	–	–	+
Middle ear	+	+	–	+	+	+

F indicates focal staining, – indicates no staining, + indicates positive staining.

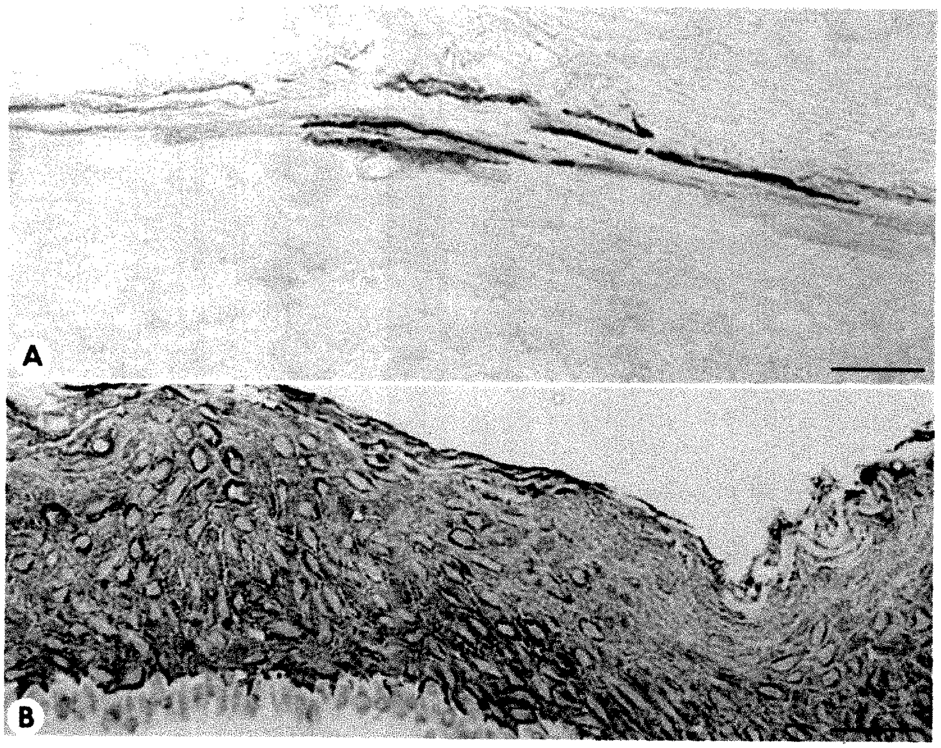

Fig 4. Cryosections of cholesteatoma. Bars — 8 μm. A) Positive staining for cytokeratin 4 in small foci, which was seen infrequently. B) Reaction product indicating presence of cytokeratin 10. Note absence of staining in stratum basale.

Results obtained for other epithelial tissues[10] strongly suggest that the morphologic differences between stratified cornifying cholesteatoma and meatal epidermis[19,20] on the one hand and the noncornifying middle ear epithelium on the other would be reflected also by a divergence in cytokeratin pattern. Our results show that although both cholesteatoma and auditory canal wall epidermis possess cytokeratin 10, this cytokeratin was not expressed by the noncornifying middle ear epithelium. This is in agreement with the data published by Moll et al,[10] who found cytokeratin 10 in cornifying stratified epidermis, eg, foot-sole epidermis and anal canal epithelium, and not in noncornifying epithelia such as that of the trachea and esophagus. The presence of cytokeratin 4, which was found by us occasionally in cholesteatoma matrix and invariably in middle ear epithelium, has been described for stratified epiglottis and esophageal epithelia.[10] Cytokeratins 18 and 19, which we found in addition to cytokeratin 4 in middle ear epithelium and in focal concentrations in some cholesteatomas, are characteristic features of a number of noncornifying epithelia such as that of the trachea. Cytokeratin 8, found in middle ear epithelium, also can be demonstrated in the trachea.

In sum, the results of the present study on the expression of cytokeratins in cholesteatoma, meatal, and middle ear epithelia are in general consistent with the cytokeratin patterns of epithelia reported in the literature, although the infrequent observation of minor focal concentrations of cytokeratins 4, 18, and 19 seems to be exceptional.

An evaluation of the cytokeratin expression of cholesteatoma matrix in relation to the cytokeratin patterns in meatal and middle ear epithelia permits three conclusions:

1. The staining characteristics of cytokeratin observed in cryosections of most cholesteatomas are similar to those seen for meatal epidermis.
2. The cytokeratin pattern in middle ear epithelium differs distinctly from the pattern occurring in most cholesteatomas.

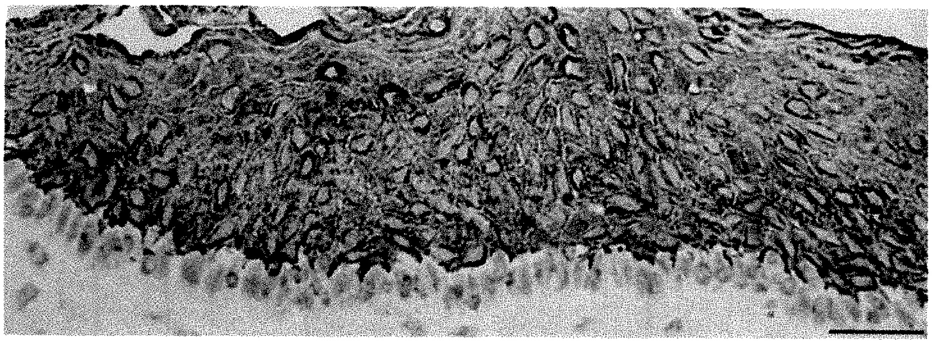

Fig 5. Immunoperoxidase staining for presence of cytokeratin 10 in meatal epidermis showed same staining characteristics as were found for cholesteatoma. Bar — 8 μm.

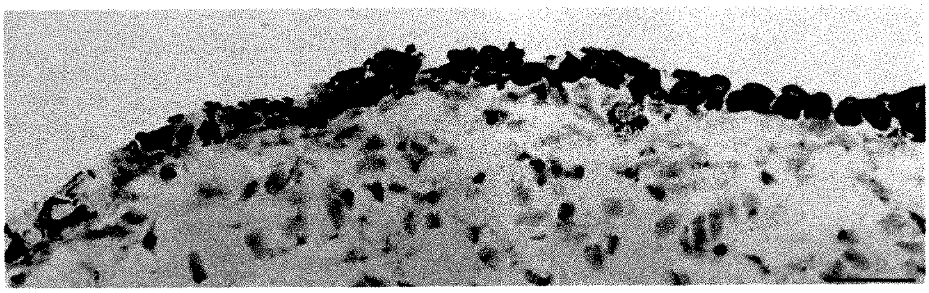

Fig 6. Cryosections of middle ear epithelium showing presence of cytokeratin 18. Bar — 8 μm.

3. Two of the cholesteatomas studied showed a minor focal presence of cytokeratins 4, 18, and 19. These cytokeratins are characteristic of middle ear epithelium and some noncornifying epithelia.

Although on this basis cholesteatoma would be expected to have a relation to auditory canal wall epithelium rather than middle ear epithelium, a metaplastic origin of cholesteatoma cannot be excluded.

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ACUTE AIRWAY OBSTRUCTION AND ACHALASIA OF THE ESOPHAGUS

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Patients with achalasia tolerate considerable distension of the esophagus. Respiratory symptoms usually are due to regurgitation and pulmonary aspiration of retained food rather than to a space-occupying mechanism. We describe a case of previously undiagnosed achalasia presenting in an elderly woman with symptoms consistent with tracheal obstruction of acute onset.

KEY WORDS — airway obstruction, esophageal achalasia, esophagus.

INTRODUCTION

The basic function of the esophagus is to provide a coordinated pathway for ingested material. It also has an important role in the clearance of regurgitated material and in the prevention of tracheobronchial aspiration and acid reflux. Abnormalities of the ordered peristaltic sequence and failure of the lower esophageal sphincter (LES) to relax sufficiently at the right time result in impaired clearance of swallowed material. Achalasia is a primary motor disorder of the esophagus characterized by manometric features of aperistalsis of the esophageal body, hypertension of the resting LES, and impaired relaxation of the LES in response to swallowing. The functional obstruction of the LES and the absence of primary and secondary peristaltic waves for bolus propagation result in retention of ingested material and dilatation and elongation of the esophageal body.[1,2] Respiratory symptoms observed in the course of achalasia arise from regurgitation and aspiration of retained food contents, rather than from the dilatation itself. Depending on the location of the maximal esophageal extension, different clinical pictures are described. The following case report describes a patient with achalasia who presented with acute airway obstruction and stridor due to extreme dilatation of the thoracic esophagus. The probable mechanisms, diagnosis, and management are discussed.

CASE REPORT

A 74-year-old woman was referred to the emergency room with complaints of acute breathlessness and stridor that followed an evening meal. A clinical diagnosis of inhaled or ingested foreign body was suggested by the referring physician. Past medical history revealed that she was in good health until 2 years prior to presentation, when she noted gradual onset of painless dysphagia and nocturnal cough. On arrival, physical examination revealed an afebrile, elderly woman in respiratory distress. Blood pressure was 160/100 mm Hg, pulse rate 130 beats/min, and respiratory rate 25/min with tracheal and sternal indrawing. Inspiratory stridor was present and diminished breathing sounds were audible over the right lung. Indirect laryngoscopy demonstrated no laryngeal disease. Stasis of saliva at the hypopharynx was noted. The diagnosis of inhaled foreign body was advanced. A portable plain posteroanterior chest radiograph revealed a shadow containing irregular mottled densities occupying two thirds of the right lung (see Figure, A). A plain lateral view of the chest demonstrated an air-fluid level located posterior to the cardiac silhouette and trachea (see Figure, B). The trachea was pushed from behind forward and compressed by a dilated fluid-containing viscus (see Figure, B [arrows]). Computed tomography of the chest performed upon admission demonstrated an extremely dilated esophagus occupying almost the entire right hemithorax. The right lung was compressed. An air-fluid level was demonstrated clearly (see Figure, C).

A diagnosis of achalasia with megaesophagus was suspected strongly. Because of increasing breathing difficulties a nasoesophageal tube was introduced blindly, evacuating 1,200 mL of fluid, semisolids, and air under pressure. Thereafter a gradual relief of breathlessness and stridor was observed. Esophagoscopy and barium radiography (see Figure, D) performed later confirmed the diagnosis of achalasia. The patient subsequently underwent Mosher bag dilatation of the LES on two occasions. This procedure provided effective relief of symptoms, and by 6 months after presentation, neither upper airway obstruction nor dysphagia had recurred.

DISCUSSION

The cause of primary achalasia has not yet been

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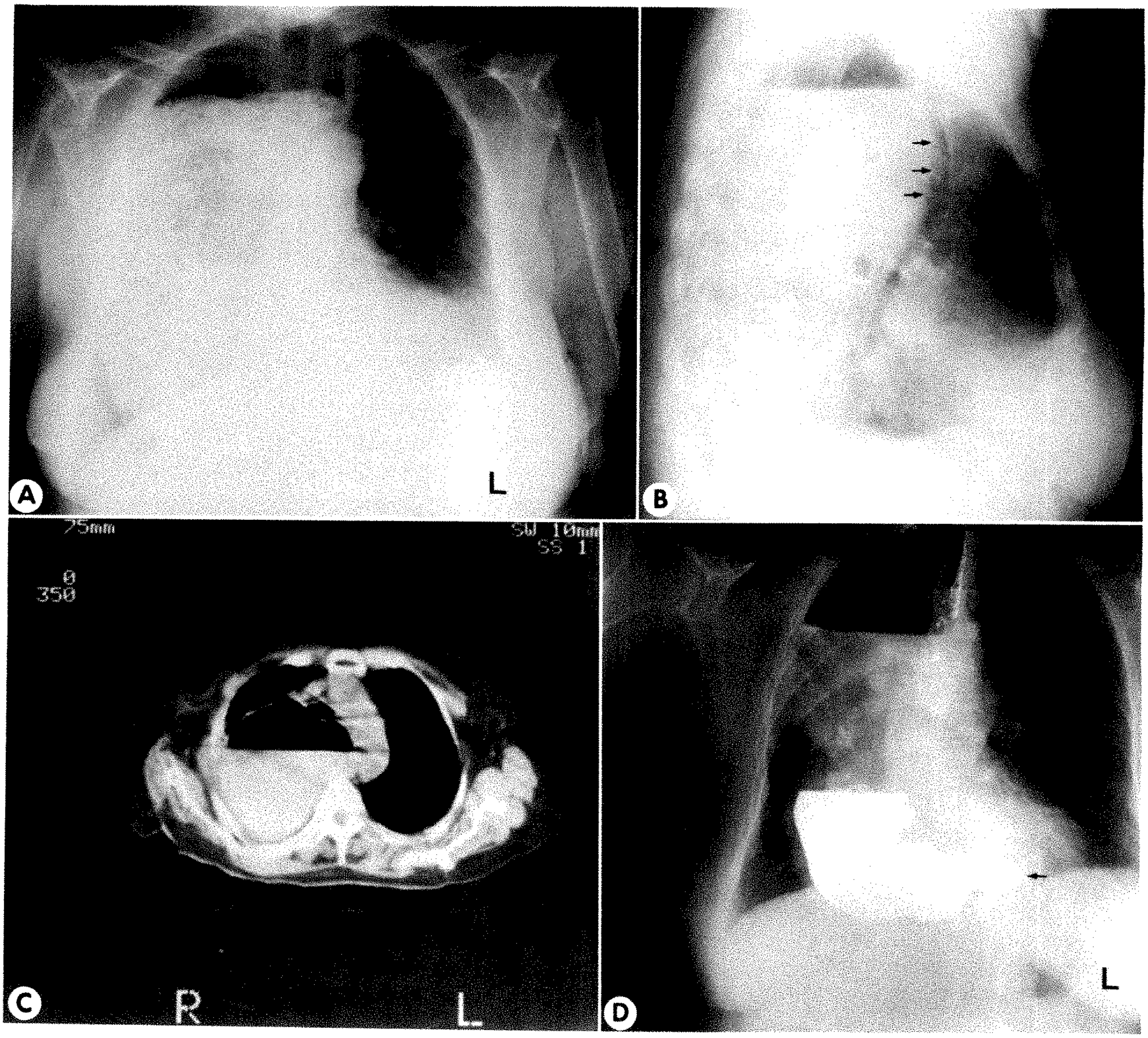

Images from patient evaluation. A) Plain posteroanterior radiograph showing shadow containing irregular mottled densities occupying most of right hemithorax. B) Plain lateral chest radiograph showing air-fluid level located posterior to cardiac silhouette and trachea. Trachea is pushed forward and compressed by dilated viscus. Arrows — compressed trachea. C) Computed tomogram of chest upon admission. Two thirds of right hemithorax are occupied by megaesophagus. Entire right lung is compressed. Air-fluid level is seen clearly. D) Barium swallow study showing mediastinal viscera as dilated amotile esophagus. Distal esophagus shows markedly tapered or "bird-beak" appearance (arrow) as barium squirts through it. These findings are typical for achalasia.

determined. Degenerative lesions have been found in the myenteric and inhibitory ganglia of the esophageal wall, vagal trunk, and dorsal vagal nuclei of the brain stem.[3-5] Secondary achalasia exhibits the same manometric features as the primary form, but for it a cause, ie, Chagas' disease or an underlying neoplasm, can be identified. Although achalasia may appear in infancy or old age, it is most common in early adult life and the prevalence has been estimated at about 1/100,000.[6] The usual presentation is of an increasing painless dysphagia for both solids and fluids. Regurgitation of retained food is likely to occur at night and, being of esophageal origin, is not sour. Respiratory symptoms are usually due to acute or chronic pulmonary aspiration rather than to a space-occupying mechanism.[7] In the more severe grades of achalasia the esophagus lengthens, often assuming a sigmoid shape as well as enlarging circumferentially. Depending on the location of the maximal esophageal enlargement, different clinical pictures are described. A dilatation confined to the cervical part may compress the cervical veins, producing the clinical picture of thoracic inlet obstruction with a low cardiac output.[8,9] A distension located in the thoracic esophagus may cause compression of the trachea and main stem bronchi from behind and may give rise to an insidious or acute-onset dyspnea and stridor.[10-17] In previous reports of acute stridor and dyspnea in achalasia, cervical or thoracic esophageal distension were attributed to an incompetent cricopharyngeal sphincter acting as a pinch-cock valve, thus allowing air entry into the atonic esophagus on inspiration but trapping it in expiration.[12,14,18]

The notable feature of our case was that the onset of symptoms was acute and followed an evening meal. Stridor and dyspnea resulted from acute compression of the trachea and the entire right lung by an extremely dilated, food-containing esophagus. Air entrapment in the course of a stressful situation contributed to further dilatation of the esophagus, exerting additional pressure on the already compressed airways. Although the primary diagnosis was that of an inhaled or ingested foreign body, prompt radiographic diagnosis and immediate decompression of the dilated esophagus prevented a possibly serious outcome. It can be argued as to whether decompression of the dilated esophagus should be performed, in cases of achalasia, through a blindly introduced nasoesophageal tube or via direct esophagoscopy. The risk of aspiration of the dilated esophageal contents during anesthesia and the presence of dysphagia and stridor may favor the use of the blind procedure. Introduction of the nasoesophageal tube, in such cases, should be performed with extreme care to avoid injury to the already atrophied esophageal walls. It must be emphasized that no medical or surgical treatment can correct the basic disorder of achalasia. Definitive therapy is aimed, therefore, at reducing LES pressure by disrupting the muscular ring at the esophagogastric junction, which is achieved by Heller esophagomyotomy or by forceful pneumatic dilation of the LES. About two thirds of patients can be relieved permanently by one or more pneumatic dilations. Surgical esophagomyotomy is associated with a more long-standing cure and a higher cure rate than pneumatic dilatation, but with a greater occurrence of postoperative gastroesophageal reflux symptoms.[19]

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FACIAL NERVE PARALYSIS WITH BENIGN PAROTID MASSES

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Facial paralysis in the presence of a parotid mass has been associated classically with a presumed diagnosis of malignancy. However, isolated case reports have documented the occurrence of paresis or paralysis secondary to pathologically benign, nonneurogenic parotid lesions. These previous cases have been reviewed and three additional cases are described. Comparisons are made on age, sex, symptoms, physical findings, pathologic findings, and prognosis. Involvement of the seventh nerve may be explained on the basis of compression, especially in association with local inflammation. Although facial paralysis still should be considered indicative of a malignancy, it also may be caused by benign masses, particularly those associated with rapid enlargement and/or infection.

KEY WORDS — benign parotid mass, facial nerve paralysis, parotid abscess.

INTRODUCTION

Facial paralysis in the presence of a parotid mass has been associated classically with a presumed diagnosis of malignancy. Eneroth[1] reviewed over 2,000 patients with parotid tumors. Facial nerve paralysis was present in 46 of these individuals; all had malignant parotid tumors.

However, Ward and Hendrick[2] in 1950 noted a paresis of the seventh nerve in a woman with a benign mixed tumor that enlarged rapidly following local trauma. Subsequently, other investigators have reported facial nerve paresis or paralysis in association with pathologically benign, nonneurogenic parotid lesions.[3-15] These cases are reviewed and three additional cases are reported.

Case 1. A 72-year-old woman was admitted to the cardiology service at the Medical Center Hospital of Vermont with a diagnosis of myocardial infarction. During her convalescence an asymptomatic swelling was noted at the right angle of her mandible, which prompted an otolaryngology consultation. On examination, a 3-cm mobile, nontender, discrete parotid mass was palpable in the right retromandibular area without facial weakness or infection.

Results of a right parotid sialogram were normal, and a thin needle aspiration biopsy revealed a degenerated, necrotic-appearing background with clusters of benign epithelial cells compatible with sialadenitis; however, a benign neoplasm could not be ruled out.

Since the patient recently had sustained a myocardial infarction, it was elected to defer any surgery until she had recovered sufficiently.

Approximately 1 month later, the patient was readmitted to the medical center for control of hypertension with a treatment protocol including diuresis. During this hospitalization, the patient developed a right-sided bacterial parotitis with the previously noted mass no longer palpable. A paralysis of the musculature supplied by the right ramus mandibularis and cervical branch of the seventh nerve was noted. She was treated for 1 week with a regimen of intravenous nafcillin sodium, hydration, warm packs, and sialogogues with minimal improvement. A computed tomogram with enhancement revealed a 4-cm mass in the deep lobe of the parotid gland compressing the internal jugular vein (see Figure, A). The measured density of the lesion was slightly less than that of muscle, and a circumferential area of increased vascularity was noted to be surrounding the mass. These findings were consistent with a diagnosis of either an abscess or a tumor. Because of the facial paralysis, it was decided to perform a parotidectomy, approaching the mass as a malignancy.

At the time of operation, the mass extended posteriorly to the upper portion of the styloid process and was adjacent to, but not adherent to, the main trunk of the facial nerve. It extended medially into the lateral pharyngeal space and anteriorly to the submandibular triangle.

The cervical and mandibular branches of the seventh nerve could be traced for approximately 1 cm beyond the pes anserinus before they became so densely encased in fibrous tissue that further identification became impossible. Postoperatively, there was a permanent paralysis of the facial musculature supplied by the aforementioned seventh nerve branches.

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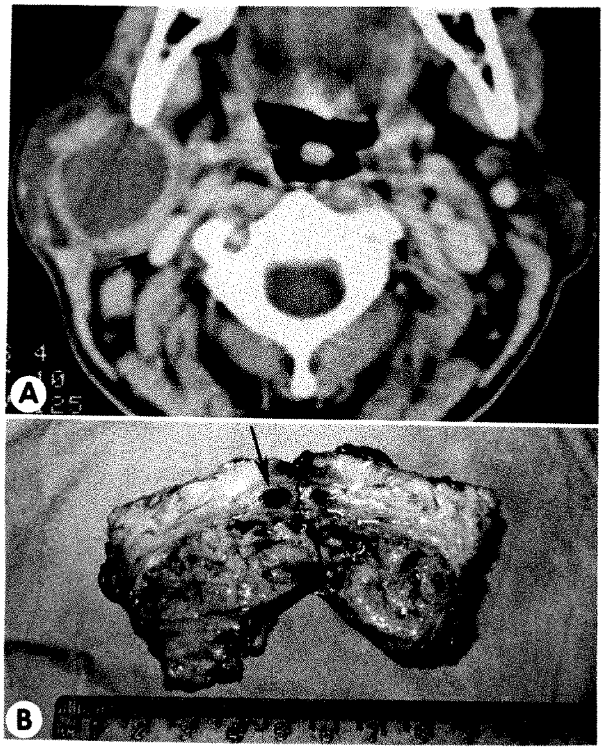

(Case 1) A) Computed tomogram showing parotid mass with enhancing capsule, compressing internal jugular vein (arrow). B) Photograph of sectioned gross specimen demonstrating well-encapsulated mass with trabeculated cavity and associated lymph node (arrow). Ruler is in centimeters.

On gross examination, the operative specimen, exclusive of the superficial lobe of the parotid, measured approximately 5.5 cm in diameter and was "shaggy," soft, and tan in color. Sectioning of this specimen revealed a well-encapsulated mass with a trabeculated cavity containing approximately 5 mL of turbid yellow-brown fluid (see Figure, B). The expected "shaggy" wall that would surround an abscessed cavity was not present.

Histologic sections revealed the cyst wall of the tumor to be papillary and to contain central lymphatic nests of cells with overlying necrotic columnar epithelium. "Ghost cells" were seen composing the epithelium. These findings are usually a result of infarction with secondary coagulation necrosis. Surrounding this tissue were areas of fibrosis, inflammation, ductal dilatation, and fat necrosis. A nerve fiber was identified in the fibrous tissue surrounding the tumor. An adjacent intraparotid node revealed follicles and ductal inclusions. On the basis of these findings, the diagnosis of a Warthin's tumor with necrosis and abscess formation was made.

The patient has no evidence of recurrent disease 5 years subsequent to surgery.

Case 2. A 38-year-old man presented with a 2-week history of a left-sided neck mass. He was treated initially with oral Keflex, 500 mg daily, with no significant response in his symptoms. He was referred to the Medical Center Hospital of Vermont after the abrupt onset of a left ramus mandibularis paralysis.

The patient denied any fever, chills, or exposure to individuals with infectious diseases. He was a 20-pack-year smoker and a mild-to-moderate drinker.

Examination revealed a 5 x 7-cm mass in the left parotid gland. There was mild trismus, and a left ramus mandibularis paralysis was evident. The remainder of his head and neck examination yielded normal findings.

A CT scan was obtained because of the question of a malignant lesion with facial nerve weakness. It demonstrated a well-circumscribed, encapsulated lesion with a low central density. The lesion was superficial to the mandible, and the medial aspects of the gland were spared of any disease.

A thin needle aspiration biopsy was undertaken and approximately 3 mL of purulent material was aspirated from the lesion. The Gram stain revealed gram-positive cocci and the culture grew a "few" *Clostridium perfringens* organisms. Results of acid-fast bacillus and fungal stains and cultures were negative. Cytologic evaluation revealed an inflammatory reaction and no evidence of malignancy.

The patient was admitted and given intravenous nafcillin sodium. A parotid abscess was drained subsequently through a modified Blair incision. The patient experienced an unremarkable postoperative course. His infectious process resolved without incident and his incision healed well. However, his ramus mandibularis paralysis persists without improvement after 4 years.

Case 3. A 75-year-old man presented with a 3-day history of a severe sore throat. On the day of his office visit he developed right-sided facial swelling and paralysis.

The patient had a history of alcoholism and had previously been treated for prehepatic coma, ascites, and bleeding esophageal varices. After abstinence from alcohol for 5 years, results of his most recent liver function studies were normal. Currently, he was taking Aldactone and Lasix for hypertension.

Examination revealed a mildly confused, slightly disoriented patient with warm, tender swelling of his right parotid gland and upper right side of the neck. A complete right-sided facial paralysis was noted. There was fullness of the right side of the soft palate. His WBC was 8,500/mm^3 with a left shift. His BUN was 29 mg/dL with a creatinine of 1.2 mg/dL. These findings and his toxic condition prompted administration of intravenous ceftizoxime sodium and surgery. Through an extended Blair incision, parotid and parapharyngeal space abscesses were drained. Subsequently, the aerobic culture grew *Klebsiella oxytoca*, and the anaerobic culture grew *Bacteroides melaninogenicus*, *Peptostreptococcus* sp, and *Fusobacterium* sp.

With the appropriate antibiotic therapy, the neck and parotid swelling gradually resolved, but the swelling in his soft palate did not change. A thin needle aspiration of the soft palate was performed on the second postoperative day, and purulent debris was obtained. With subsequent aspirations of the palate, the inflammation resolved, and the palate appeared symmetric by the seventh postoperative day.

The patient's hospital stay was prolonged because of multiple medical complications; he was discharged on the 21st postoperative day.

Some facial function was noted by the second postoperative day. By 1 month, the forehead area was still weak, but he had symmetric function of the middle and lower face. At 1 year he had complete recovery without synkinesis or dyskinesis.

DISCUSSION

Benign masses of the parotid gland rarely are associated with facial nerve symptoms. In fact, there are only 17 reported cases of histologically benign, nonneurogenic masses in the English literature.[2-15] Of these, benign mixed tumors (four), parotid cysts (four), and parotid abscesses (four) represent the majority of these lesions, comprising 71% of the total cases. Three Warthin's tumors, one alveolar duct malformation, and one oncocytoma account for the rest. The size ranged from 0.5 to 7.0 cm, with a mean of approximately 3.5 cm. The histology, size, and duration of the lesions did not correlate with severity or with recovery of facial nerve function. There was no instance of invasion of the nerve by any of these benign neoplastic processes.

The predominant age group was in the fifth to seventh decades of life, with an average age of 61 years and a range of 9 to 77 years. There was a 1.8:1 male to female ratio, with 65% of the patients being male.

The most commonly described findings are presence of a mass in 13 cases (76%), pain in 12 cases (71%), diffuse swelling of the parotid gland in 11 cases (65%), and enlargement of a preexisting mass in six cases (35%).[2-15] Ninety-four percent of the patients were noted to have either a mass in or swelling of the parotid gland associated with their seventh nerve dysfunction, with the range of duration being from 1 week to 1 year. Many patients had a history of both swelling and a mass. Greater than 70% of the patients experienced pain prior to the deterioration of their facial nerve function; this symptom is associated classically with malignancy.

The majority of the patients had total involvement of the facial nerve branches. When partial involvement was noted, the ramus mandibularis, either by itself or in combination with other branches, was affected most commonly. Seventy-six percent of the patients had paralysis, with the remainder having paresis. There was no relation between the severity and the extent of nerve involvement.

The pathogenesis of facial nerve dysfunction related to benign masses of the parotid gland has been conjectured in various case reports in the literature as being due to a variety of factors, including pressure on the nerve trunk by tumor,[5,8,10,13] kinking of the nerve as it enters the firm parotid fascia,[5] and infection.[9,14] The effect of local toxic factors, in those cases in which infection was present, cannot be refuted or confirmed with the available information. In those cases without infection, pressure on or kinking of the nerve would be the most likely explanation of the facial nerve dysfunction, especially when associated with rapid enlargement of the mass. Although a history of rapid enlargement of the mass was elicited in only a third of the patients, it was probably undetected in many instances in which inflammation and diffuse swelling were present. This mechanism also could be the cause of the facial nerve dysfunction in patients with parotid abscesses (cases 2 and 3), due directly to the mass effect of the rapidly expanding abscess — especially if the nerve was entrapped in the fibrous, inflamed area immediately surrounding the abscess.

In case 1, the presence of the tumor itself was not enough to cause facial nerve dysfunction. The Warthin's tumor may have caused ductal obstruction, similar to that in a case reported by Cross.[13] Obstruction, along with a diuretic-induced dehydration at the time of the second admission, probably caused the bacterial parotitis with tumor necrosis. The subsequent rapid enlargement of the intralesional cavity compressed the lower divisions of the facial nerve, which had become trapped in the surrounding areas undergoing inflammatory and fibrous reactions.

All of the lesions were treated surgically, with 76% of the cases reported having at least partial recovery of facial nerve function. Return of facial nerve function took longer in those patients with paralysis than those with paresis. Logic would dictate that the less severe the dysfunction, the more likely the recovery. However, neither the severity or the extent of the initial nerve involvement, nor the presence of infection, correlated with the degree of return of facial nerve function. This apparent discrepancy may have its origin in the extent of surgery that was required for each particular case. The more extensive the seventh nerve dissection, the greater the chance of trauma. Therefore, the degree of facial nerve recovery would depend not only on the nature of the disease process but also on the amount of surgical trauma. In the case reported by Mamakos et al,[10] the nerve was sectioned in the fallopian canal to allow for complete removal of the tumor; it was reconstructed subsequently with a greater auricular nerve graft.

The rarity of these cases is such that facial nerve paralysis in the presence of a parotid mass should still be considered an indication of malignancy. However, benign mass-lesions also can cause seventh nerve dysfunction, especially if associated with rapid enlargement and/or infection.

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AMERICAN AUDITORY SOCIETY

The 16th annual meeting of the American Auditory Society will be held in New Orleans on Sunday, September 24, 1989. The meeting is scheduled in conjunction with the annual meeting of the American Academy of Otolaryngology - Head & Neck Surgery. For further information, contact J. W. Hall III, PhD, Department of Otolaryngology, School of Medicine, Vanderbilt University, Nashville, TN 37232.

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TYPE II COLLAGEN DISTRIBUTION IN THE EAR OF THE GUINEA PIG FETUS

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By using monoclonal antibodies to type II collagen and immunohistochemical techniques, we studied the distribution of type II collagen in the developing guinea pig ear. Type II collagen appearance and disappearance corresponded to cartilage development and resorption. Type II collagen was identified in Meckel's and Reichert's cartilages, the cartilage plate of the auricle and external acoustic meatus, the ossicles, eustachian tube cartilage, and the otic capsule. Type II collagen also appeared with the development of structures in noncartilaginous parts including the tympanic membrane, tympanic annulus, basilar membrane, spiral limbus, spiral ligament, and osseous spiral lamina, Rosenthal's canal, the maculae of the utricle and saccule, and the semicircular canal membrane, crista ampullaris, and endolymphatic duct. Type II collagen is distributed widely in the ear after the early stages of development. Thus, type II collagen should be considered an important structural component of the ear.

KEY WORDS — cartilage, guinea pig ear, monoclonal antibodies, type II collagen.

INTRODUCTION

The molecular heterogeneity of collagen has been well established in recent years, and at least 12 genetically distinct collagens (types I through XII) have been identified in mammalian tissues.[1] Although none of the collagen types is uniquely tissue specific, characteristic tissue distributions, arising embryonically in precisely programmed patterns, have been noted. Type I, III, V, and VII collagens are widely distributed in various connective tissues, and type II, IX, X, and XI (1α, 2α, 3α) collagens are mainly restricted to cartilage. Type IV collagen is abundant in basement membrane.[1] Type VIII collagen, originally identified in the medium of cultured endothelial cells, was identified recently in Descemet's membrane.[2]

Upon determining where and when the collagens appear, the physiologic functions and pathologic potential of the individual collagens can be studied. The distribution of type II collagen in the adult human inner,[3] middle, and external ear[4] has been reported by our laboratory. A possible role for type II collagen autoimmunity in the pathogeneses of otosclerosis, Meniere's disease, and eustachian tube chondritis[5-11] has been suggested. Levels of antibodies to type II collagen were significantly greater in the sera of patients with otosclerosis and Meniere's disease than in those of control subjects.[5] In animal experiments, cochlear hydrops and spiral ganglion cell degeneration have been induced in guinea pigs by immunization with native type II collagen.[6] Furthermore, rats immunized with native type II collagen showed neurosensory hearing loss associated with spiral ganglion cell degeneration, vestibular dysfunction,[7] otospongiosislike lesions,[8] and eustachian tube chondritis.[10] Immunohistochemical studies demonstrated IgG and C3 deposits in ear tissues suggesting an autoimmune response to type II collagen.

Previous studies have characterized the pattern of type II collagen synthesis during embryonic development. Once thought to be found only in hyaline cartilage,[12] type II collagen is also synthesized by three chick embryonic tissues — notochord,[13] corneal epithelium,[14] and neural retina epithelium[15] — and by the developing murine otic capsule.[16] Reports evolving from some of these studies have suggested that type II collagen might be involved causally in certain epitheliomesenchymal interactions eliciting cranial skeletogenesis.[17]

No reports, however, have yet described collagen synthesis during chondrogenic differentiation in the embryonic guinea pig. The purpose of this study is to chronicle the appearance and distribution of type II collagen throughout the developing fetal guinea pig ear.

MATERIALS AND METHODS

Six strain 13 pregnant guinea pigs were killed painlessly on days 20, 30, and 50 after mating to ob-

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From the Departments of Medicine (Ishibe, Cremer, Yoo) and Microbiology and Immunology, the Neuroscience Program, the Divisions of Allergy-Immunology and Connective Tissue Diseases, University of Tennessee, Memphis (Yoo), and the Veterans Administration Medical Center, Memphis (Cremer, Yoo). This research was supported by medical research funds from the Deafness Research Foundation, the American Otologic Society, Inc, and the Veterans Administration. This study was performed in accordance with the PHS Policy on Humane Care and Use of Laboratory Animals, the NIH *Guide for the Care and Use of Laboratory Animals*, and the Animal Welfare Act (7 U.S.C. et seq.); the animal use protocol was approved by the Institutional Animal Care and Use Committee (IACUC) of the University of Tennessee, Memphis. Dr Ishibe is currently at the Department of Otolaryngology, Kansai Medical University, Osaka, Japan. Dr Cremer is the recipient of an Arthritis Investigator Award from the Arthritis Foundation.

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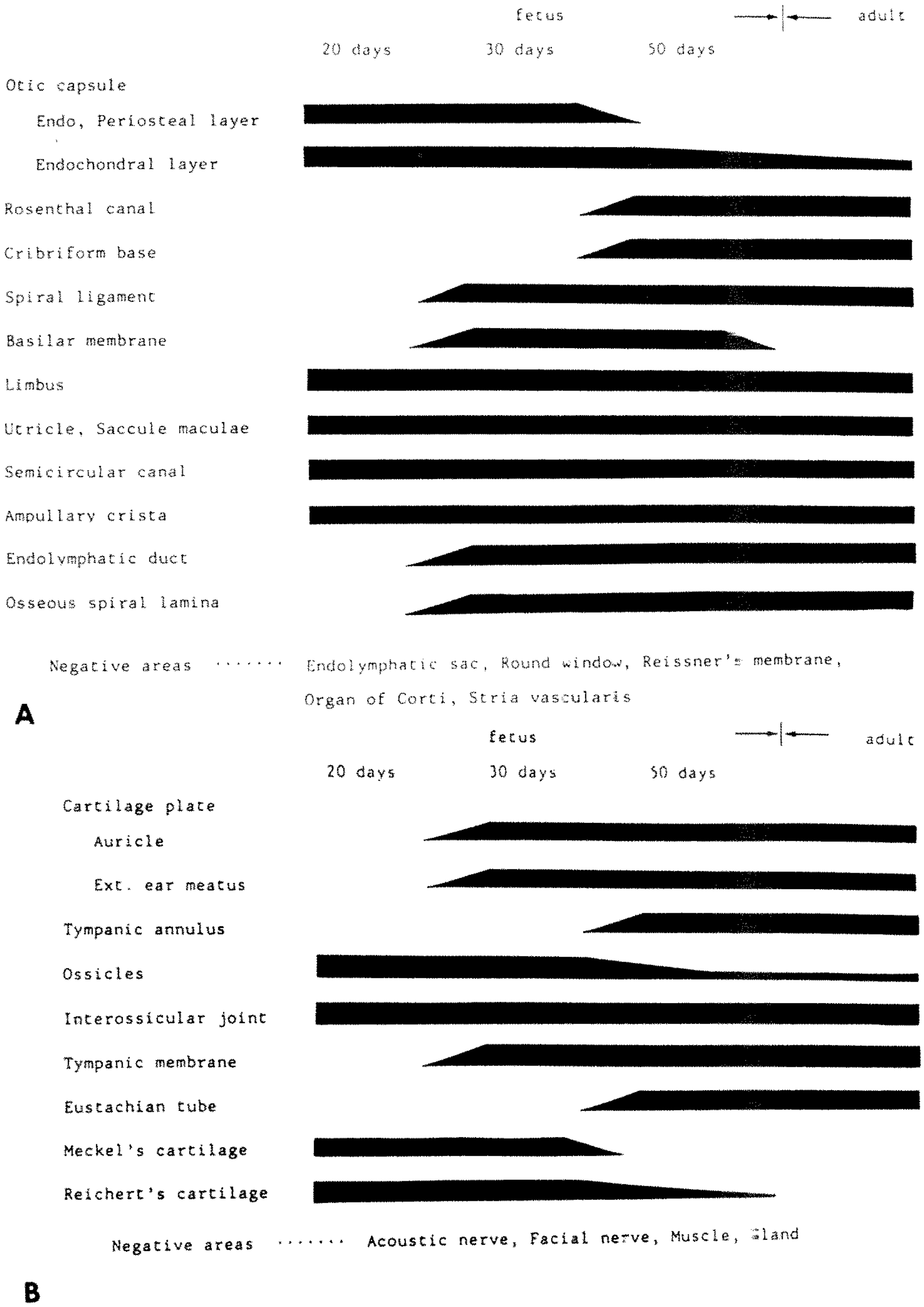

Fig 1. Scheme of type II collagen development in guinea pig. Closed bars show presence of type II collagen. A) Inner ear. B) Middle and external ear.

tain the fetuses representing early, middle, and late developmental stages, respectively. Two adult guinea pigs (weight 200 to 250 g) also were studied. Fetal ages were confirmed by reference to weight and size tables.[18] The gestation time of normal guinea pigs is approximately 64 days.

Monoclonal antibody to type II collagen was produced in mice by hybridoma technique based on the principle described by Köhler and Milstein.[19] Type II collagen was isolated and purified from chick sternal cartilage as described by Trelstad et al.[20] DBA/1J mice were immunized with native chick type II collagen (50 μg/mouse) emulsified with an equal volume of complete Freund's adjuvant. Lymph nodes and spleen were isolated on day 14, 48 hours after a booster injection of collagen and incomplete adjuvant. Hybridoma lines were formed by fusing lymphocytes and SP2/0 myeloma cells with polyethylene glycol. Monoclonal antibody-producing hybridomas were selected by culture in medium containing hypoxanthine, aminopterin, and thymidine and identified with an enzyme-linked immunosorbent assay system using type II collagen-coated microtiter wells. A clone (E9) was identified by limiting-dilution assay that reacted with chick type II collagen and cross-reacted with guinea pig type II collagen. A subclone, designated E5, was derived from E9 but differed in that it no longer reacted with type II collagen. Neither E9 nor E5 reacted with type I, III, IV, V, IX, or XI collagens.

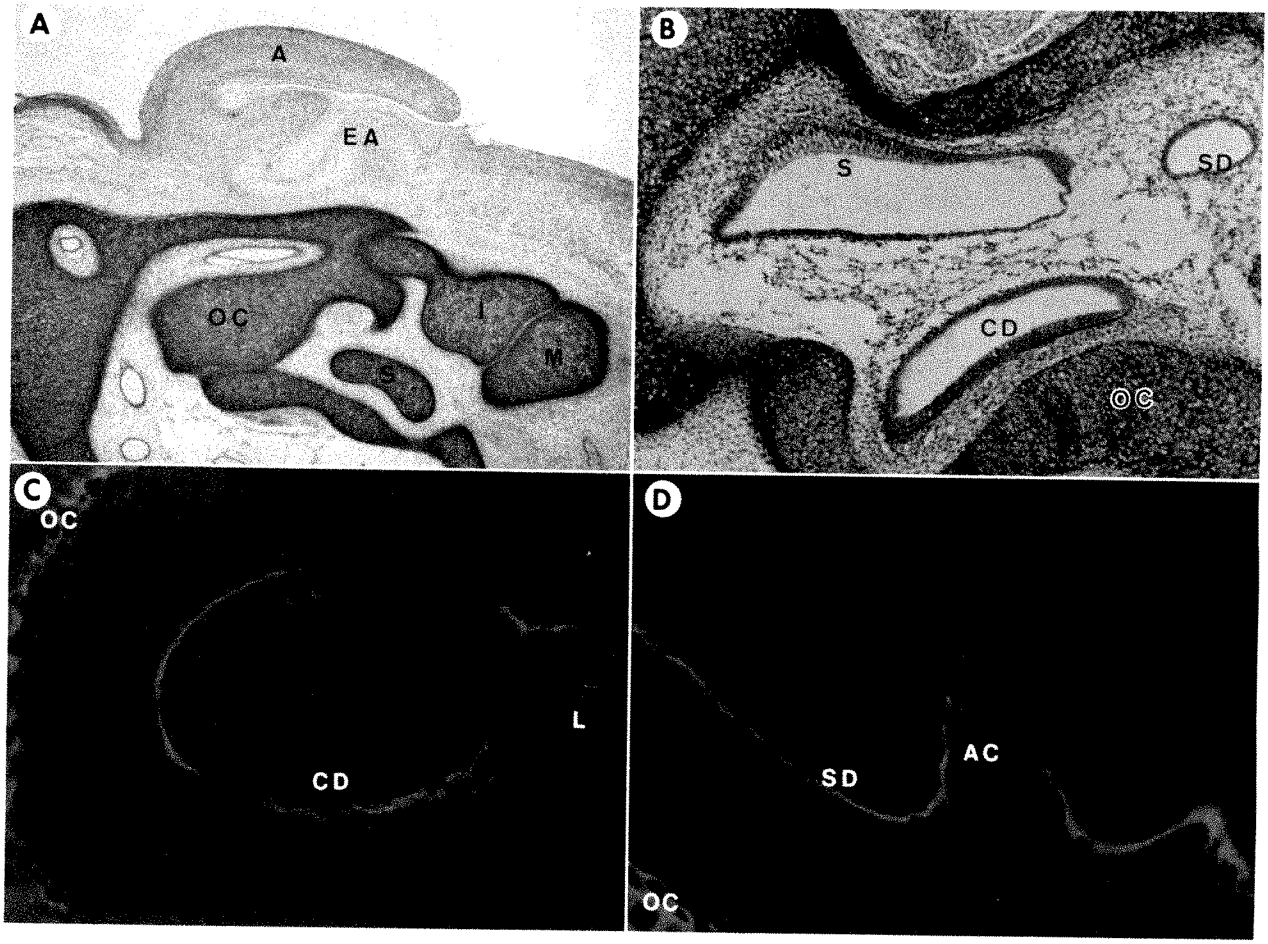

Fig 2. Type II collagen in ear of 20-day-old guinea pig fetus. A) Positive immunoperoxidase staining and hematoxylin counterstaining in primitive otic capsule (OC), malleus (M), incus (I), and stapes (S), but not in external auditory canal (EA) or auricular cartilage (A) (original x21). B) Positive immunoperoxidase staining and hematoxylin counterstaining in primitive otic capsule (OC), semicircular duct membrane (SD), subepithelial area of primitive cochlear duct (CD), and saccule (S) (original x60). C) Indirect fluorescence micrograph of cochlea showing type II collagen in primitive otic capsule (OC), subepithelial area of primitive cochlear duct (CD), and primitive limbus area (L) (original x115). D) Indirect fluorescence micrograph showing type II collagen in otic capsule (OC), subepithelial area of ampullary crista (AC), and semicircular duct membrane (SD) (original x180).

For immunohistochemical studies, we modified slightly a paraffin-embedding technique described by Sainte-Marie.[21] Temporal bones were removed, fixed in cold 95% ethanol, decalcified with 5% EDTA solution (pH 7.4) at 4°C, and then embedded in melted paraffin at 56°C. Sections were cut horizontally at 7 μm and dried overnight at room temperature. Deparaffinized sections were treated with testicular hyaluronidase to degrade proteoglycans that mask type II collagen.[21] Nonspecific background staining was reduced by incubation with a 1:5 dilution of normal goat serum in 1% bovine serum albumin dissolved in phosphate-buffered saline (PBS). Endogenous peroxidase was blocked with 0.5% hydrogen peroxide in methanol. Ascites fluid rich in E9 monoclonal antibody, which cross-reacted with guinea pig type II collagen, was used as a first antibody after dilution in PBS (1:1,000). Either fluorescein isothiocyanate or peroxidase-conjugated goat anti mouse IgG (1:20 dilution) was used as a second antibody. Normal mouse serum, monoclonal antibody to chick type II collagen preincubated with soluble chick type II collagen, ascites fluid produced by subclone E5, and mouse anti *Streptococcus* M protein monoclonal antibody were used as negative controls. Articular cartilage from a normal guinea pig was used as a positive substrate control.

RESULTS

A schematic overview of the development of type II collagen in inner, middle, and external ear is shown in Fig 1. The closed bar shows the presence of type II collagen.

Type II collagen was identified in the following areas of the guinea pig ear by immunofluorescence and immunoperoxidase staining techniques.

In the 20-day fetus (early stage) (Fig 2), it was identified in the primitive ossicles and primitive otic capsule (Fig 2A); the macula utriculi and macula sacculi (Fig 2B); the primitive limbus area, Meckel's cartilage, Reichert's cartilage, and the subepithelial

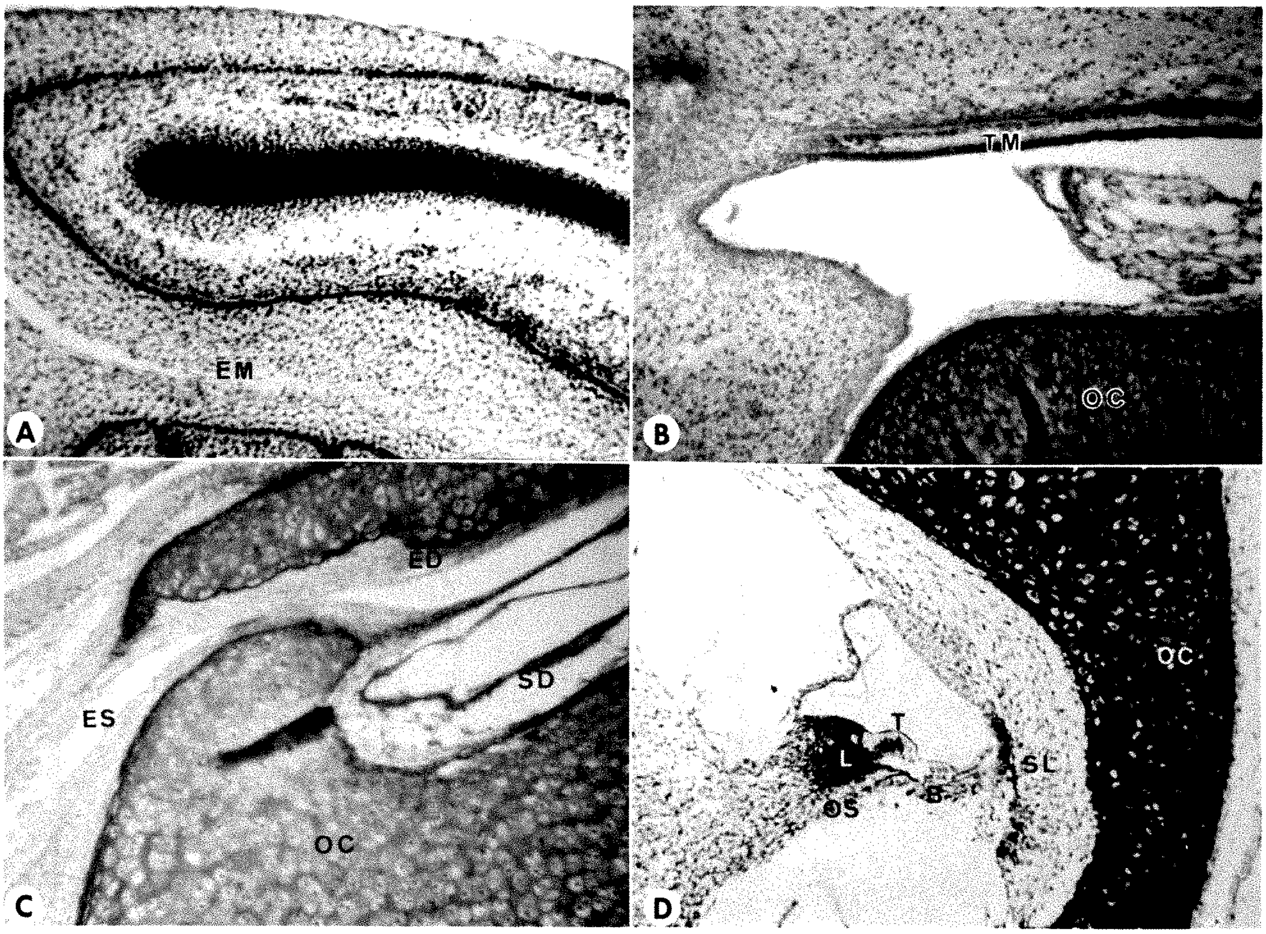

Fig 3. Type II collagen in ear of 30-day-old guinea pig fetus (original x60). A) Positive immunoperoxidase staining in cartilage plate around external acoustic meatus (EM). B) Positive immunoperoxidase staining and hematoxylin counterstaining in primitive otic capsule (OC) and tympanic membrane (TM), but not in tympanic annulus. C) Positive immunoperoxidase staining and hematoxylin counterstaining in otic capsule (OC), subepithelial area of endolymphatic duct (ED), and semicircular duct membrane (SD), but not in endolymphatic sac (ES). D) Positive immunoperoxidase staining and hematoxylin counterstaining in primitive otic capsule (OC), limbus (L), basilar membrane (B), osseous spiral lamina (OS), part of spiral ligament (SL), and tectorial membrane (T).

layer of the primitive cochlear duct (Fig 2C); and the semicircular canal membrane and ampullary crista (Fig 2D).

In the 30-day fetus (middle stage) (Fig 3), in addition to the 20-day fetal findings, type II collagen was identified in the cartilage plate in the auricle and around the external acoustic meatus (Fig 3A); the tympanic membrane (Fig 3B); the endolymphatic duct (Fig 3C); and the limbus, a portion of the spiral ligament, the osseous spiral lamina, and the basilar membrane (Fig 3D). At this stage, the primitive cochlear duct had changed and almost all structures of the future cochlea were identifiable.

In the 50-day fetus (late stage) (Fig 4), in addition to the 30-day fetal findings, type II collagen was found in the tympanic annulus and the endochondral layer and globuli ossei in the otic capsule (Fig 4A); the interossicular joint (Fig 4B); the eustachian tube cartilage (Fig 4C); and Rosenthal's canal and the cribriform base (Fig 4D). Type II collagen decreased in the ossicles, the otic capsule, and Reichert's cartilage in the 50-day fetuses because of their ossification. Type II collagen was not observed in Meckel's cartilage at this late stage.

In adults, type II collagen was seen in the same areas as in the 50-day fetus, except that it was absent in adults in the basilar membrane and Reichert's cartilage. Type II collagen was not observed throughout fetal development in the endolymphatic sac or round window, Reissner's membrane, or the organ of Corti, stria vascularis, nerves, muscles, skin, or salivary glands. None of the negative control sections showed specific staining. Articular cartilage served as the positive substrate control and always showed positive staining.

DISCUSSION

To elucidate the function of a collagen type, it will be useful to describe its spatial and temporal appearance in developing and adult tissue. The present study was designed to map the onset and patterns of type II collagen synthesis in the developing guinea pig ear. Use of monoclonal antibody, reacting to a single antigenic site on the type II colla-

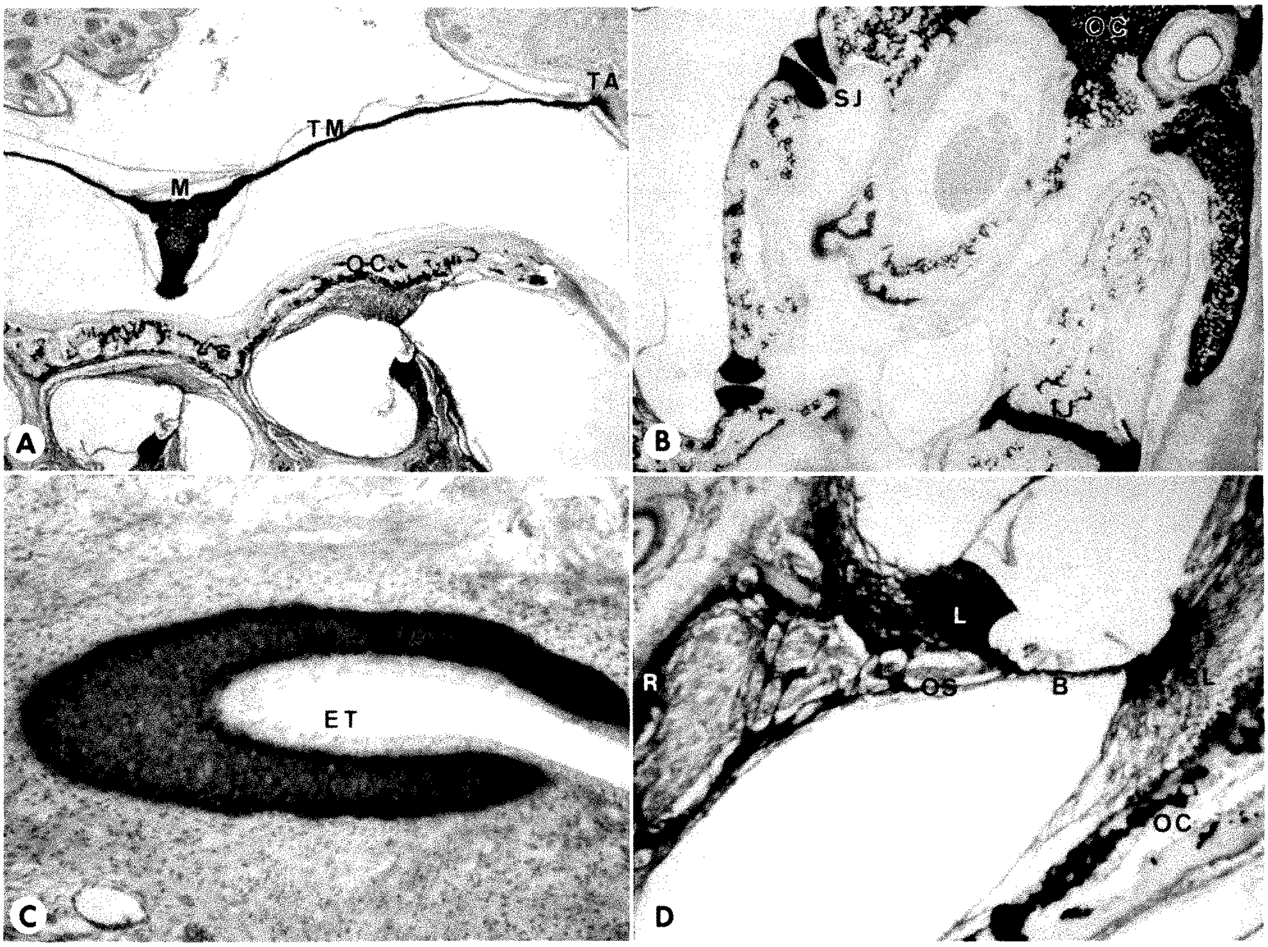

Fig 4. Type II collagen as shown by positive immunoperoxidase staining in ear of 50-day-old guinea pig fetus. A) In tympanic membrane (TM), malleus (M), tympanic annulus (TA), and endochondral layer of cochlear otic capsule (OC) (original x21). B) In interossicular joint (IJ), stapediovestibular joint (SJ), and otic capsule (OC) (original x60). C) In eustachian tube cartilage (ET) (original x60). D) In Rosenthal's canal (R), limbus (L), basilar membrane (B), spiral ligament (SL), osseous spiral lamina (OS), and endochondral layer of otic capsule (OC) (original x60).

gen molecule, assured the purity of the results.

The cartilaginous neurocranium in the developing head of all vertebrates serves as a pattern for the formation of the bony skull. Along this line, the cartilaginous otic capsule is the precursor of the bony portion of the inner ear. The otic capsule arises during chondrogenesis from cephalic mesenchyme of both neural crest and mesodermal origin.[22,23] Studies with amphibians,[24-26] birds,[27] and mice[28] have revealed conclusively that chondrogenic differentiation is induced by developmental interactions between the periotic mesenchyme and its neighboring epithelia, the otocyst and the rhombencephalon. D'Amico-Martel et al,[16] using mice embryos, and Thorogood et al,[17] using chick embryos, have revealed that type II collagen is expressed transiently in the periotic mesenchyme while the above interactions are taking place. Thorogood et al[17] suggest that this transient expression might be causally involved in the periotic epitheliomesenchymal relationship. This morphogenetic hypothesis for type II collagen is supported by the fact that disruption of collagen secretion by L-azetidine-2-carboxylic acid alters murine otic extracellular matrix production, which in turn affects the above discussed interaction, leading to dysmorphogenesis of the inner ear.[29] Thorogood et al[17] further postulated that in the chick embryo, type II collagen expression may dictate where and when chondrogenesis-promoting interactions will take place for the entire developing chondrocranium.

We have presently shown that type II collagen is expressed transiently in the primitive otic capsule of the developing guinea pig, supporting the above observations of D'Amico-Martel and Thorogood. However, its distribution is much more extensive than this, as it appears widely throughout the ear during the early, middle, and late stages of embryonic development. The distribution of type II collagen in the 50-day fetus (late stage) is almost identical to that observed in the adult, except that it is absent in the adult in Reichert's cartilage and the basilar membrane. Type II collagen appearance corresponded with the growth and resorption of the following cartilaginous structures: Meckel's cartilage, Reichert's cartilage, the cartilage plate of the auricle and external acoustic meatus, the ossicles, the eustachian tube cartilage, and the otic capsule. It should be noted that type II collagen also appeared in the tectorial membrane (Fig 3D). This supports our previous observation in adults that human cochlear tectorial membrane binds anti–type II collagen antibody[3,30] and the recent observation by Thalmann et al[31] that the tectorial membrane is rich in type II collagen. Type II collagen also appeared with the development of the following other noncartilaginous structures: tympanic membrane, tympanic annulus, limbus, spiral ligament, osseous spiral lamina, basilar membrane, Rosenthal's canal, maculae of the utricle and saccule, semicircular canal membrane, ampullary crista, and endolymphatic duct. Thus, in addition to having a proposed inductive influence on the developing inner ear, type II collagen serves as an extensive component of the entire ear. With this in mind, could type II collagen also have an amorphogenetic role in the developing middle and external ear?

With the baseline data of the present report, future studies dealing with embryonic development can be performed on developing guinea pigs. The developmental deformities of osteogenesis imperfecta involve a defect in or absence of type I cartilage.[32] The deafness usually related to otosclerosis occurs in many families with osteogenesis imperfecta.[33] Could the production of type II collagen be absent or altered in congenital internal as well as external ear malformations? Future comparison of the present data with patterns of collagen production by mutant or experimentally manipulated fetal guinea pig ear tissues can be made to investigate hypotheses such as these. Also, the possible role of type II collagen autoimmunity in otosclerosis has been described.[9,11] It has been suggested that endochondral rests, containing type II collagen, from the embryonic otic capsule might be involved in this autoimmunity.[11] Knowledge of the onset and distribution of type II collagen in the developing embryo thus may shed some light on the pathogenesis of this prevalent and disabling disorder.

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NIH THERAPEUTIC STUDY OF FOLLICULAR THYROID CARCINOMA

The National Institutes of Health request the cooperation of physicians in referring patients with pure follicular thyroid cancer for a randomized clinical trial that will investigate the effectiveness of radiosensitizing agents in enhancing radioiodine therapy. Patients should have had primary thyroid surgery, without additional therapy for recurrences, and meet one of the following criteria: 1) age 40 years or older at the time of diagnosis with either primary tumor greater than 3 cm, regional lymph node metastases, extensive tumor capsule penetration, or extensive angioinvasion; or 2) any age with either tumor penetration into surrounding tissues or metastases outside of the neck.

All medical care expenses at NIH will be covered by the government except for transportation costs. Physicians will be informed regularly about the status of their patients and will continue to provide long-term care for them. Please write or telephone Dr Kenneth B. Ain or Dr Jacob Robbins, Bldg 10, Rm 8N315, National Institutes of Health, Bethesda, MD 20892; (301) 496-2831 or (301) 496-5761.

Ann Otol Rhinol Laryngol 98:1989

IMAGING CASE STUDY OF THE MONTH

HEMANGIOMA OF THE ZYGOMATIC BONE

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Primary hemangiomas of bone are exceedingly rare neoplasms. They account for only 0.7% of all osseous neoplasms.[1] Although they make up 10% of the primary benign tumors of the calvarium, they comprise only 0.2% of the osseous neoplasms of the skull.[1]

The first case of hemangioma of bone was reported by Toynbee[2] in 1845. It was not until 1950 that Schofield[3] reported a case of hemangioma of the zygoma. Careful scrutiny of the case reveals that this lesion was a hemangioma that secondarily invaded bone. The first true documentation of a hemangioma of the zygoma was in 1961 by Sherman and Wilner,[4] who reviewed all of the available records from Memorial Sloan-Kettering Hospital.

CASE REPORT

A 38-year-old woman presented with pain and swelling over the lower lateral orbital rim and malar eminence that had lasted for 4 months. There was no history of antecedent trauma. The remainder of her medical history was unremarkable.

Her physical examination discovered a well-circumscribed, tender 3.5 x 2-cm bony mass involving the left orbital rim and zygoma. The overlying skin was erythematous but freely mobile.

Results of laboratory studies were within normal limits. Routine facial bone radiographic findings were inconclusive because of the superimposed paranasal sinuses. A computed tomographic scan revealed a rarefied, monostotic, well-circumscribed region in the left malar eminence that expanded the outer and inner cortex of bone (see Figure, A). The history, findings of the physical examination, and radiographic evidence were consistent with a diagnosis of fibrous dysplasia.

The patient was explored via an extended brow incision. A well-demarcated, "bluish," encapsulated tumor of the zygomatic bone was discovered below the zygomaticofrontal suture. Biopsy of the lesion resulted in hemorrhage controlled by bone wax and firm local pressure. Postoperatively, a magnetic resonance scan yielded findings consistent with a vascular tumor of the left zygoma (see Figure, B). There was a mixed signal in the left zygoma as well as a local, linear lack of signal on the anterior surface of the mass. The lesion was isointense with muscle on the T1-weighted images and hyperintense on the T2-weighted images. Pathologic examination revealed tissue that consisted of normal-appearing bone with dilated intertrabecular spaces. These spaces contained benign fibroconnective tissue with vessels consistent with bony hemangioma (see Figure, C). The patient underwent an en bloc excision of the tumor with primary reconstruction of the orbital rim with a free iliac bone graft. Intraoperatively the lesion was found inferior to the zygomaticofrontal suture, bowing the outer and inner cortex of the zygoma. The zygomatic process of the frontal bone was uninvolved by tumor.

The patient did well postoperatively, with abatement of her symptoms. Five months later, contouring of the bone graft was necessary to reduce a bony overhang. She is doing well 1 year postoperatively, with no evidence of disease.

DISCUSSION

Hemangiomas of bone are found primarily in the vertebrae. In a study of 2,154 vertebrae there were found 257 hemangiomatous tumors of bone.[1] Excluding vertebral bodies, the skull is the most commonly affected area of the body. Within the skull, the parietal bones are affected most commonly, followed by the frontal bones (46% versus 23%).[1] Other commonly affected facial bones include the mandible, maxilla, and nasal bones.[5] Within the skull base, the occiput and petrous portion of the temporal bones have been affected.[1]

Bony hemangiomas are found most commonly in the fourth decade (22.5%), followed by the second (17.5%), third, and fifth (10%). The average age in Wyke's study[1] was 29.8 years of age. Case reports include patients from 3 weeks to 70 years of age (cited by Wyke[1]). A female predilection of 3:1 has

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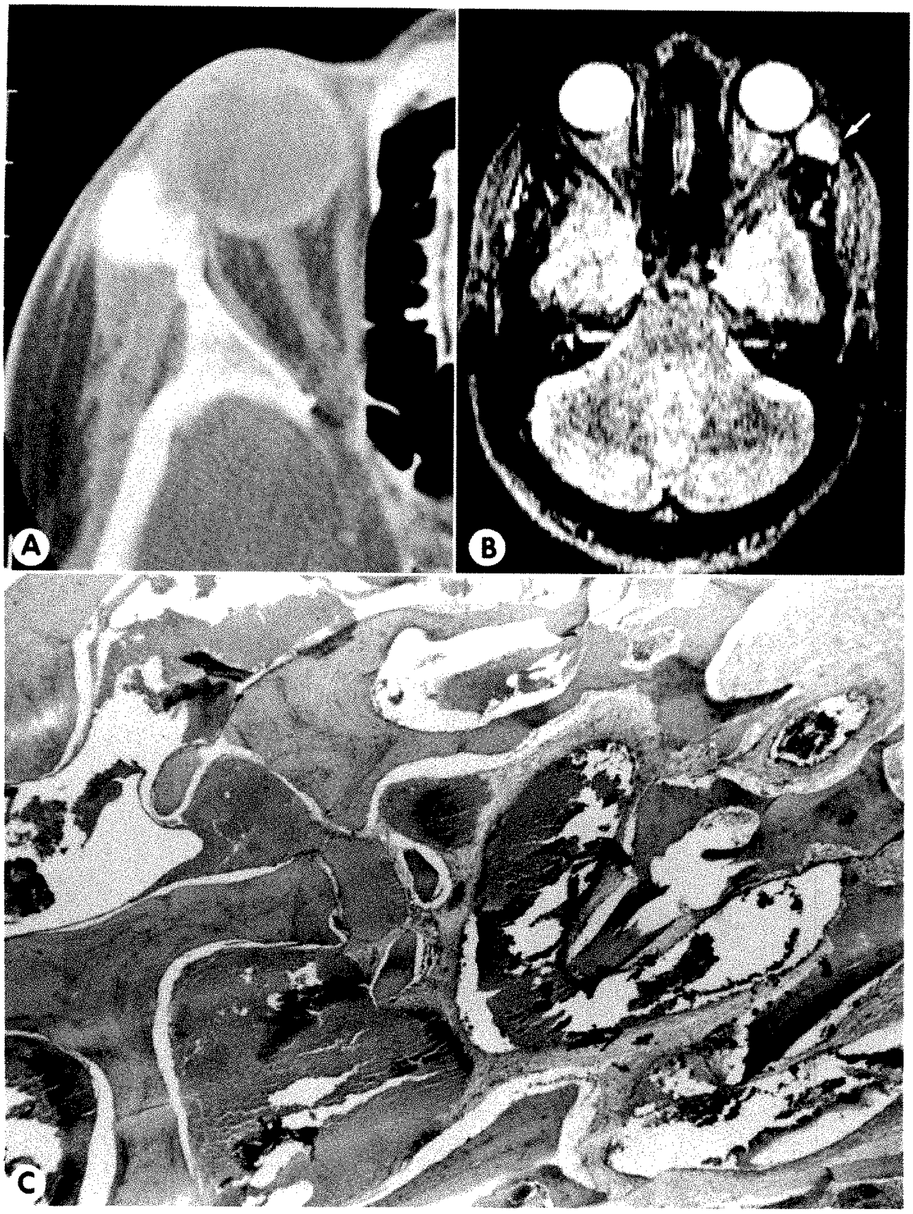

Hemangioma of zygomatic bone. A) Computed tomogram of left malar eminence demonstrating amorphous, highly dense enhancing mass in orbital process of zygoma. B) Magnetic resonance image (T2-weighted) showing well-delineated vascular blush in region of left zygomatic bone (arrow). C) Histologic section showing mixed capillary-cavernous pattern (H & E).

been found,[5] although other studies found no such trend.[1] Bony hemangiomas rarely are found in blacks.

The American College of Surgeons classifies angiomas of bone as a variety of tumors of nonosteogenic origin. Two types are described, one arising from blood vessels within bone and affecting bone primarily, and one originating from blood vessels of the periosteum that secondarily invade the marrow. Toynbee[2] felt that the origin of bony hemangiomas was related to centers of ossification within the bones. Wyke[1] and Davis and Morgan[6] showed that there was no statistical relationship to suggest this hypothesis. Another theory is based on the observation of antecedent trauma to the bone prior to the formation of the bony lesion.[5] Fifty percent of nasal bone hemangiomas have been associated with antecedent trauma.[7]

The location of a bony hemangioma determines its symptoms. Often the history is nonspecific, the most frequent complaint being a hard mass that has been present for months to years. The overlying soft tissue is mobile.[1] Tenderness may be present, but pain is less frequent. Bony hemangiomas of the zygoma may cause deformity of the cheek and/or orbit.[5] Since these lesions expand only the outer cortex of bone,[8] focal neurologic findings are uncommon until late in their course. Bruits are rare.[8]

Grossly these lesions appear as hard, blue to violet domed masses lying beneath periosteum.[1] The bone is spongy in appearance.[9] Histologically, two types of hemangioma can be distinguished — capillary and cavernous.[5] Capillary hemangiomas are rarely encountered in the calvarium, the majority of reported cases being cavernous.[1] Both types have been found in the zygoma.[5,6] The capillary type

TABLE 1. RADIOGRAPHIC DIFFERENTIAL DIAGNOSIS OF BONY HEMANGIOMAS

Findings	*Possible Diagnoses*
Striations	Hemangioma (radial); meningioma (parallel); osteogenic sarcoma
Osteolysis	Metastatic disease; multiple myeloma; hemangioendothelioma
Multifocal sites	Histiocytoses; metastatic disease; multiple myeloma; hemangioendothelioma
Palpable mass	Hemangioma; fibrous dysplasia; osteoma

consists of fine capillary loops spreading outward in a sunburst fashion. The cavernous lesion consists of large blood-filled lacunae embedded in a connective tissue matrix and lined by large flattened endothelial cells. These may arise from diploic veins. The osseous matrix lies outside the fibrocellular matrix that encloses the endothelium-lined spaces. The bony trabeculae are continuous with the osseous tissue of the parent bone, with an orderly pattern to the lamellae.[1] Abundant osteoblasts and osteoclasts indicative of active bone remodeling can be seen. Remodeling is a response to the neoplasm's presence. Degenerative and necrotic changes have been seen in the osseous matrix secondary to the outstripping of the blood supply in older tumors. No phleboliths have been observed in the vascular spaces in any blood vessel tumors of bone.[1]

The first radiographic description of an osseous hemangioma was in 1917.[10] In 1949 the first correct preoperative diagnosis was made of a cranial hemangioma.[1] Classically, in flat bones a sunburst or wheel-spoke appearance is seen, whereas in long bones a soap bubble or honeycomb appearance is noted.[11] When viewed tangentially, calvarial flat bones containing hemangiomas will exhibit the sunburst pattern with bony spicules radiating from the center of a rarefied circular defect.[12] This appearance is due to the expanding neoplasm that draws apart and compresses the bone elements, resulting in bone remodeling.[13] The shape of the lesion is round or oval. The margins of the defect are sharp and well delineated, with no osteosclerosis.[4] Frequently, expansion of the outer cortex is noted.

The above characteristics facilitate the radiographic diagnosis when the lesion is in the calvarium. The anatomic complexity of the facial skeleton does not allow easy radiographic diagnosis of bony hemangiomas, because of overlapping of sinuses and cranial structures.[11,14] Computed tomography often shows an expansile lytic process with a high-density, enhancing, amorphous mass that may be suggestive of fibrous dysplasia.[15] Magnetic resonance imaging is extremely accurate in making the diagnosis of these lesions. Because of its low flow state, bony hemangioma appears as a blush in a region occupied by bone. No bone windows are necessary, since MRI does not enhance bone.

Any lesion of bone that is lytic and round by radiographic criteria should be suspected to be a bony hemangioma. The differential diagnosis is extensive (Table 1).

These lesions do not undergo malignant degeneration, nor do they involve regional lymph nodes. In fact, bony hemangiomas' benign nature is suggested by their often long and protracted course.[1] Left untreated, however, the lesion may impinge on vital structures or extend into the cranium. This is especially true of orbital and petrous bony hemangiomas. Less deleterious effects of untreated bony hemangiomas include ulceration of the overlying skin with necrosis and subsequent infection.[1] Thus, indications for treatment may include mass effect, hemorrhage, and cosmesis.[11]

The treatment of bony hemangiomas differs from that of subcutaneous hemangiomas, since sclerosing agents are impossible to use in bone.[16] Radiation therapy, curettage, and surgical excision are proven modalities of treatment.[17] Although curettage has been used successfully,[18] the potential morbidity of uncontrolled hemorrhage is too great. Radiation therapy has been shown to stop the progression of disease, but does not alter the cosmetic deformity left by the lesion.[6] Jaffe[19] believed that irradiation should be the primary mode of treatment for calvarial and skeletal hemangiomas. Reports exist of

TABLE 2. RESULTS OF PREVIOUSLY REPORTED CASES OF BONY HEMANGIOMA OF ZYGOMA

Author	*Patient Age/Sex*	*Swelling**	*Side*	*Pain or Tenderness*	*Type*
Sherman and Wilner[4]	46/F	Yes (2 yr)	Left	No	?
Marshak[5]	53/F	Yes (1.5 yr)	Right	Yes	Capillary
	35/F	Yes (1 yr)	Left	Yes	Capillary
Davis and Morgan[6]	47/F	Yes (2 yr)	Left	Yes	Cavernous
Dorfman et al[12]	?	?	?	?	?
Schmidt[18]	43/F	Yes	Right	No	?
Walker and McHenry[21]	40/F	Yes (4 yr)	Left	Yes	Capillary
	10/F	Yes (8 wk)	Left	Yes	Capillary
Har-El et al[22]	60/M	Yes (2 yr)	Right	Yes	Cavernous
Present study	39/F	Yes (4 mo)	Left	Yes	Cavernous

There were no reported cases of hemorrhage.

? — no available information.

*Times in parentheses indicate duration of swelling.

malignant degeneration of benign bony neoplasms following radiation therapy.[20] Radiation therapy may cause tissue necrosis, retardation of bone and tooth growth, and telangiectasis. However, irradiation may be useful when other modalities fail, when lesions are not amenable to excision (eg, petrous hemangiomas), or when the patient is not medically stable for surgery.

Some authors promote angiography and embolization prior to surgery.[11,14] Davis and Morgan[6] advocate ligating the external carotid artery on the involved side. Others have pointed out that ligation of feeding vessels has not altered subsequent blood flow.[14] En bloc excision includes a rim of normal-appearing bone around the tumor. This avoids severe hemorrhage and helps prevent recurrence.[21]

There are ten reported cases of bony hemangioma of the zygoma, including ours (Table 2).[4-6,12,18,21,22] The report of Schofield[3] was omitted because the evidence points to a nonosseous origin of the hemangioma. The case referenced by Dorfman et al[12] was not documented; therefore, calculations do not include this case. The average age of the patients was 41.4 years, with a female preponderance of 8:1. A left-sided tendency also was noted. Symptoms included swelling in 100% of the cases. Only two patients gave a prior history of trauma,[18,21] but seven of them complained of pain or tenderness. Hemorrhage was never reported. Pathologic findings were available on seven patients. Three of these seven had a cavernous hemangioma, as opposed to the capillary variety. All were treated by surgical excision.

SUMMARY

Bony hemangiomas of the zygomatic bone are rare. This report represents the tenth citing in the literature. The most common signs and symptoms include swelling and pain or tenderness. Diagnosis can be made by plain radiographic studies followed by CT scanning or MRI. The treatment of choice is surgical excision with a rim of normal bone around the tumor. Malignant degeneration has not been reported unless radiotherapy had been used.

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PATHOLOGY CONSULTATION

EPITHELIOID SARCOMA

JOHN G. BATSAKIS, MD
HOUSTON, TEXAS

Epithelioid sarcomas are histogenetically and often biologically peculiar soft tissue malignancies that may be either primary or metastatic in the head and neck. The sarcomas have high recurrence and metastatic rates and a sometimes torpid course but nonetheless poor survival.

Epithelioid sarcoma is a histogenetically enigmatic neoplasm of the deep dermis, subcutaneous tissues, fascia, and tendon sheaths with a predilection for the extremities of young adults.[1-3] Manifesting a tendency to propagate along fascial planes, the sarcoma may have a deceptively indolent behavior that is belied by a high rate of local recurrence, a high incidence of regional lymph node involvement, and a frequent occurrence of distant metastases.[1]

Always unencapsulated, epithelioid sarcoma may be confused histologically with a variety of benign and malignant neoplasms — a testimony to its appearance and changes with progressive disease. Differential diagnosis includes necrobiotic granuloma (rheumatoid nodule, necrobiosis lipoidica), nodular fasciitis, benign or malignant fibrous histiocytoma, synovial sarcoma, achromatic melanoma, and squamous cell carcinoma. The tendency to become less recognizable in recurrences or metastases has led Chase and Enzinger[1] to caution that a review of all pathologic material is mandatory for diagnosis.

Epithelioid sarcomas rarely are encountered as primary neoplasms in the head and neck, and because of this the clinicopathologic diagnostic difficulties can be compounded. Only 1% of 241 cases studied at the Armed Forces Institute of Pathology presented initially in the head and neck soft tissues, while 95% were located in the extremities.[1] It has been suggested that for patients younger than 15 years, this predilection is weakened.[4] In the head and neck, the scalp, ears, face, and neck have been the recorded primary sites.[1,4]

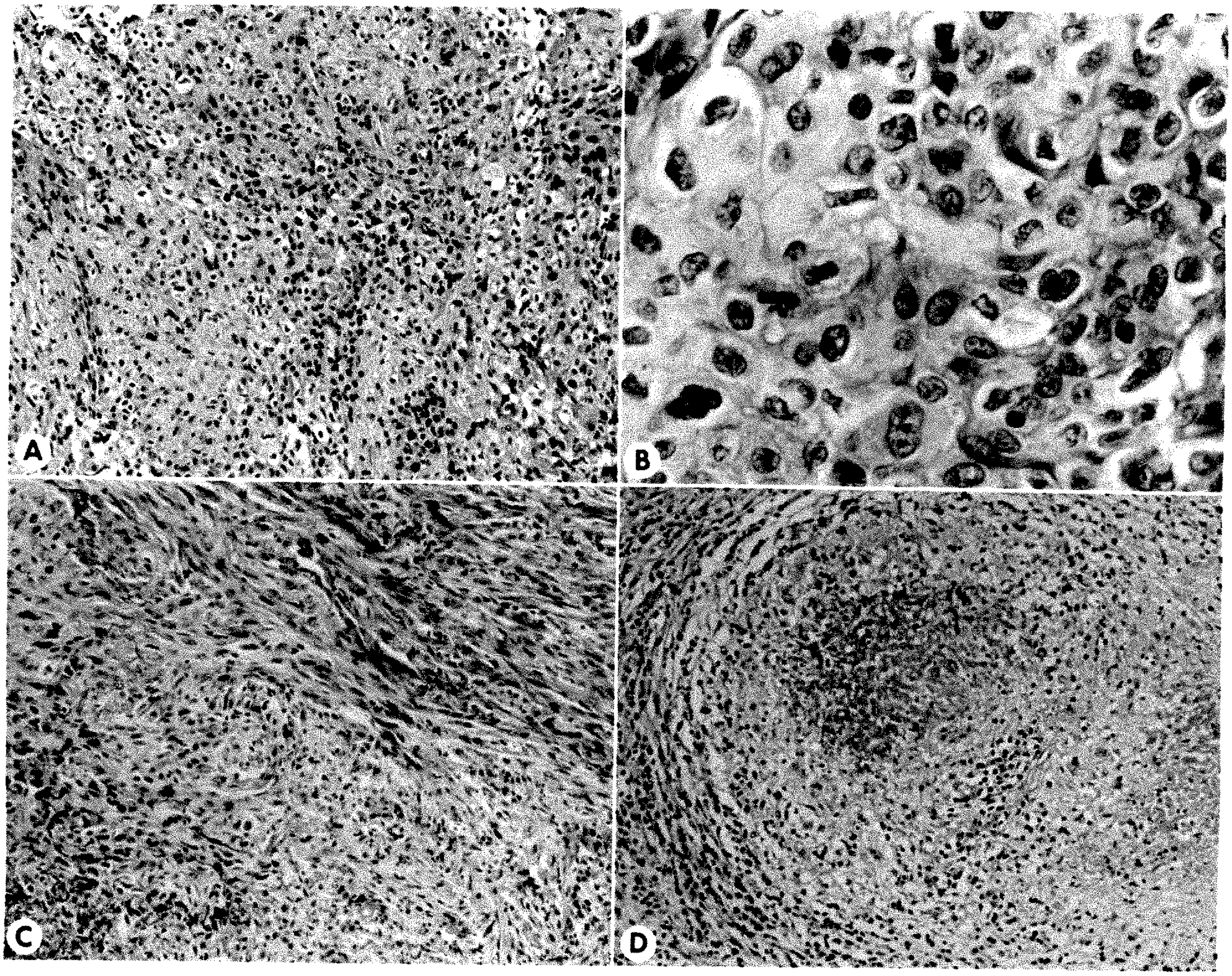
The lesional tissue is a nodular proliferation of plump, eosinophilic and epithelial-like cells that often blend subtly with fusiform neoplastic cells (see Figure, A-C). Many cells contain intracytoplasmic vacuoles. Mitotic figures are found easily, and intercellular collagen usually is prominent. The amount of necrosis influences patterns of growth.[1] A pseudogranulomatous display is most recognizable, with a proliferation of polygonal cells in a mantle arrangement around a central necrotic or relatively acellular zone (see Figure, D). Such a geographic effect is generally not found in tumors with a diffuse, nonnecrotic cell proliferation. Calcification, particularly in necrotic foci, a variably dense inflammatory reaction, and osseous and/or cartilaginous metaplasia are ancillary findings. Multinucleated giant cells are infrequent.

Electron microscopic, enzyme histochemical, and immunochemical studies all raise the possibility that this peculiar neoplasm takes origin from an epithelioid mesoblastic tissue capable of producing a sarcoma with a phenotype more often associated with an epithelial neoplasm.[1-4] Immunoreactivity of the neoplastic cells with antibodies against cytokeratins, epithelial membrane antigen, and vimentin supports this premise. Epithelioid sarcomas are nonreactive with antibodies for myoglobin, factor VIII-related antigen, and leukocyte common antigen. They may exhibit positive immunoreactions for desmin, protein S-100, and neuron-specific enolase. Whether these reactions indicate multidirectional differentiation or only nonspecificity of the antibody-antigen reaction is not known.

There is much less ambiguity over the biologic behavior of epithelioid sarcoma. It is a neoplasm with considerable lethal potential and high local recurrence and metastatic rates. Observations that the metastatic rate is higher than the death rate also reflect the paradoxically indolent behavior sometimes seen with epithelioid sarcomas.[1] In 202 patients with follow-up data, recurrences were recorded in 77%.[1] These were often multiple, tended to present within 6 months of the first surgical removal, and required a mean of 2.3 additional resections.[1] Forty-five percent of the study population manifested metastases, initially to regional lymph nodes.[1] Over half of the patients with metastases eventually had pulmonary involvement, and in 25% the lungs were the first site of metastases.[1]

From the University of Texas M. D. Anderson Cancer Center, Houston.

REPRINTS — John G. Batsakis, MD, Division of Pathology, University of Texas M. D. Anderson Cancer Center, 1515 Holcombe Blvd, Houston, TX 77030.



Epithelioid sarcoma (H & E). A) Of soft tissues of neck (original x45). Nodules of neoplastic epithelial-like cells, with some cells exhibiting vacuolated cytoplasm. B) Higher magnification of cells shown in A (original x250). Note abnormal mitotic figures. C) Showing spindle and epithelial-like cells (original x45). D) Assuming necrobiotic granular appearance (original x45). Lesions such as this can mislead and delay therapy.

Metastases to skin, especially the scalp, rank behind those to lymph nodes and lungs, and these are followed by those to bones, brain, and liver. Distant metastases are not necessarily preceded by either local recurrence or metastases to lymph nodes.[1]

Combined surgery and radiation therapy has been successful in decreasing the local recurrences, but follow-up periods have been too short to evaluate its effect on survival.[5] Sixty percent of patients dying of this disease do so within 7 years of diagnosis, but the event may be delayed for as long as two decades.[1] Overall survival has ranged from 59% (5-year actuarial) to 48% (7-year actuarial).[5]

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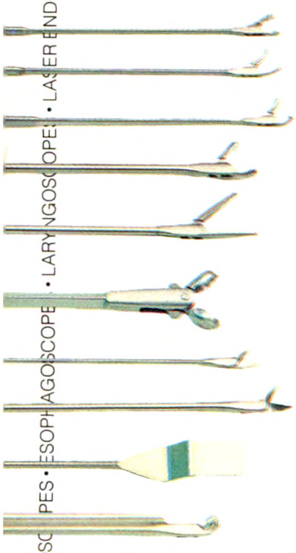

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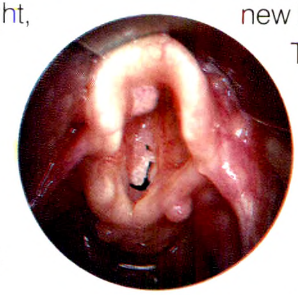

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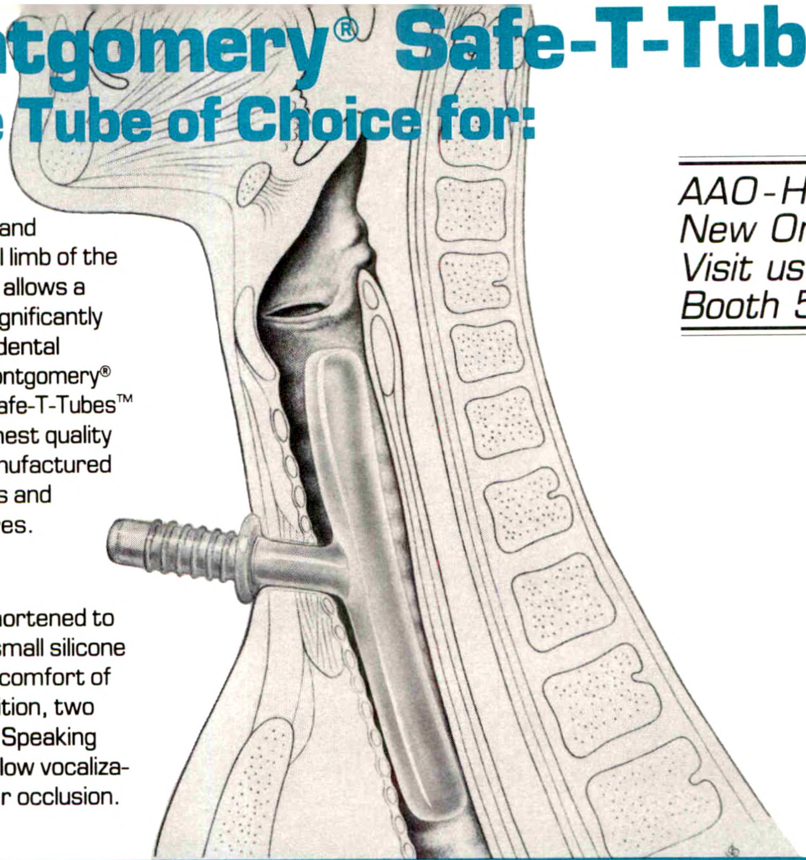

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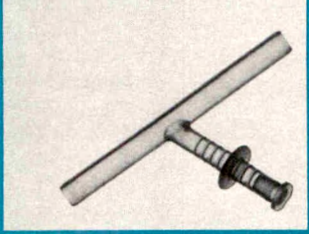

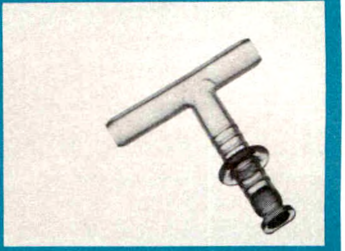

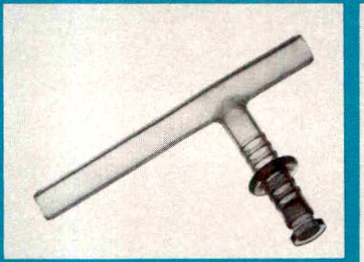

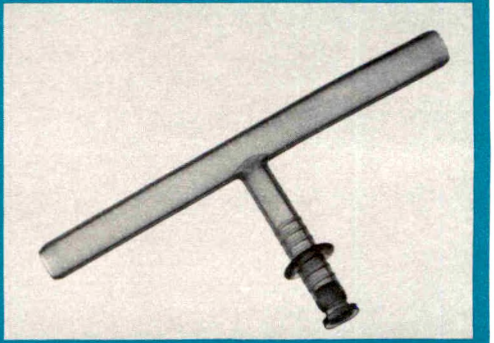

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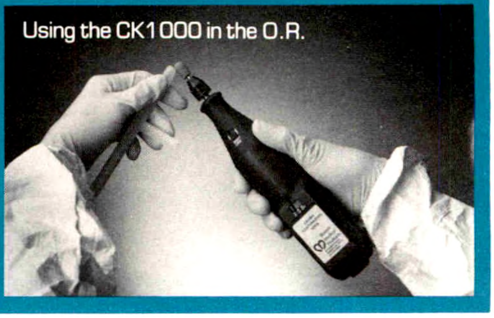

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FIFTEENTH DANIEL C. BAKER, JR, MEMORIAL LECTURE

WHAT HAVE WHOLE ORGAN SECTIONS CONTRIBUTED TO THE TREATMENT OF LARYNGEAL CANCER?

JOHN A. KIRCHNER, MD
NEW HAVEN, CONNECTICUT

The study of whole organ sections of laryngectomy specimens has demonstrated the patterns by which cancer spreads from one part of the larynx and hypopharynx to another. These studies have also demonstrated the fibroelastic membranes and ligaments that form the boundaries of intralaryngeal compartments within which cancer is confined in its early stages. They thus have added support to the concept of partial laryngectomy for selected lesions and have illustrated the features of those types of laryngeal cancer that have not responded well to radiotherapy. Whole organ sections of laryngectomy specimens have allowed a more accurate interpretation of preoperative computed tomography and magnetic resonance imaging and have provided a reliable basis for clinical staging.

KEY WORDS — cancer, laryngectomy, pathology, whole organ sections.

Although the overall cure rate for laryngeal cancer is in the 60% range, it is obtained by treatment regimens that are often inappropriate and, in many cases, needlessly radical. Tumors that might have been cured by laser excision, conservation surgery, or radiotherapy are subjected too often to total laryngectomy. Other tumors resectable by relatively minor surgical procedures are treated by radiotherapy, so that if failure occurs, the extent of residual disease is difficult to determine. Most radiotherapy failures, for this reason, end up with total laryngectomy.

To preserve the functions of the larynx and pharynx while treating cancer in these areas requires a detailed understanding of the patterns in which cancer grows and spreads in this part of the human anatomy. Most of this knowledge has been gained through a study of whole organ sections of the laryngectomy specimens that then have been compared with the tumors' preoperative appearance on laryngoscopy, computed tomography, and magnetic resonance imaging. Whole organ sections show how the lesion invades various components of the larynx, and how one part of the larynx relates to another.

A major difficulty that faces the surgeon or radiotherapist in planning treatment is the assessment of a tumor's three-dimensional volume, its extent of subsurface spread, and its possible destruction of the thyroid and cricoid cartilages that make up the laryngeal framework. Invasion of the framework, for example, is an adverse prognostic feature associated with an increased incidence of regional metastasis[1] and decreased patient survival.[2] Apart from metastasis, the foregoing features of the primary lesion are of utmost importance in planning treatment. The surgeon must be able to predict the likelihood of safe margins if the larynx is to be partly removed, and the possibility of preserving the protective mechanism of the residual larynx. The radiotherapist must estimate tumor volume and the likelihood of anoxic cells within a lesion that extends deeply under the surface of visible tumor, both of which are important factors in a tumor's response to radiation therapy.

Modern CT helps in delineating the extent of tumor, but the technique is hampered by variations in ossification patterns within the laryngeal framework. Continued improvements in MRI may eventually circumvent some of these problems. Meanwhile, however, whole organ sections of laryngectomy specimens have helped to clarify some of the problems that frequently face the clinician in diagnosing and treating cancer of the larynx and hypopharynx.

MATERIALS AND METHODS

After the laryngectomy specimen is examined by the surgical pathologist, it is photographed for the permanent record. Until the past 2 years, all specimens were processed in celloidin, according to the technique described by Tucker and Smith.[3] More recently, specimens have been processed in paraffin, which yields satisfactory sections much sooner and at considerably less expense. After the sections are available for study, the various features of the tumor's growth patterns are analyzed and coded for computer storage and retrieval. There are now 442 serially sectioned surgical specimens in the Yale collection. Some of the clinical problems that these studies have clarified are presented.

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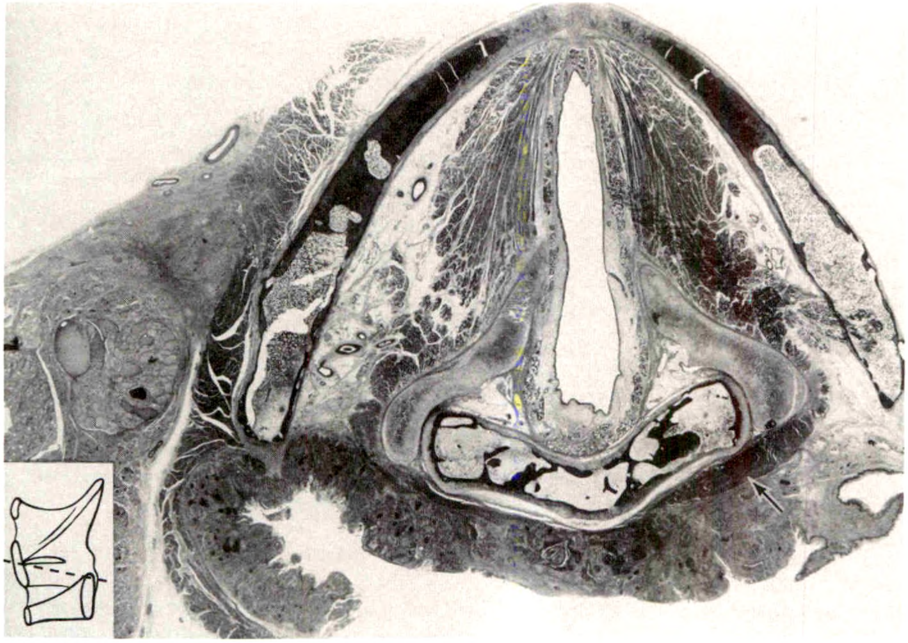

Fig 1. Transverse section of postcricoid cancer infiltrating left posterior cricoarytenoid (PCA) muscle. Left vocal cord had been motionless near midline, with no clinical evidence of cancer. Right PCA muscle shows no invasion (arrow), as cancer is limited by muscle fascia.

STAGING

Between 1964 and 1979, clinical staging was found to be inaccurate in 40% of our surgical specimens studied by whole organ section.[4] The inaccuracy was nearly always one of underestimation, usually due to invasion of the laryngeal framework or to spread of cancer into the preepiglottic space.

During the past 10 years, the incidence of staging errors has dropped to 22% in the 108 specimens sectioned, with a sharp decline in understaging. This improvement can be credited largely to the study of whole organ sections, which have helped the clinician identify those lesions whose surface appearance reflects a high probability of deep invasion, framework destruction, or extension of cancer into the preepiglottic space. Overstaging still occurs in large, overhanging tumors of the ventricular band that hide the true vocal cord from view and appear to be transglottic in location, but leave the fundus of the ventricle free of cancer. Such lesions are difficult to evaluate even by imaging techniques.

SLUGGISH VOCAL CORD

Cancer extending laterally along the superior surface of the true vocal cord may bind it to the thyroid cartilage without invading the paraglottic space. More often, a bulky tumor in this location may impair the cord's mobility by its mere size.[5] Limited mobility, however, compromises the prognosis in most cases of glottic cancer, especially if the lesion is not actually verrucous or frankly exophytic.

IMMOBILE VOCAL CORD

One must distinguish between the cord that is fixed as the result of cancer's having invaded its substance, and the cord that is merely immobile and shows no evidence of glottic cancer. This latter condition may be the result of pyriform sinus cancer's having invaded the recurrent laryngeal nerve or, more often, of postcricoid cancer's having infiltrated the posterior cricoarytenoid muscle itself[6] (Fig 1). The lesion in the hypopharynx may occasionally be difficult to identify because of its relatively small size or its location behind the cricoid plate. An edematous arytenoid cartilage is sometimes the only other clue to its presence.

Cancer that invades the cricoarytenoid joint nearly always invades the adjoining musculature and has not been observed, in our specimens, to be an isolated cause of vocal cord immobility.

FIXED VOCAL CORD

Much more often, the fixed vocal cord indicates infiltration or destruction of the thyroarytenoid muscle, with invasion of the paraglottic space. As cancer advances within this compartment, its downward spread is controlled in large degree by the conus elasticus medially and the perichondrium of the thyroid ala laterally. As a result, the growth sometimes extends beyond the larynx through the cricothyroid membrane.[7]

CANCER AT ANTERIOR COMMISSURE

Anterior commissure cancer should be assigned to one of two groups, each group differing in its potential for deep invasion. Whole organ studies have shown that if the lesion remains confined to the level of the glottis, with mobile vocal cords (T1b), it is not deeply invasive and does not invade the underlying thyroid cartilage. It is limited in its anterior extent by the dense mass of fibroelastic tissue at the anterior attachment of the true cords

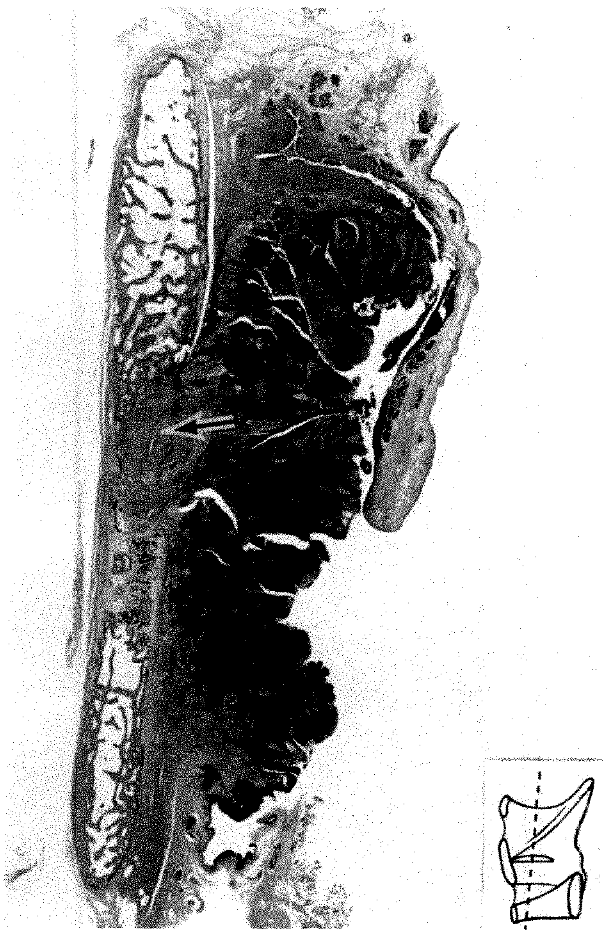

Fig 2. Coronal section of cancer occupying ventricle and extending upward under overlying false vocal cord. Both laryngeal and ventricular surfaces of false cord are free of cancer. Lesion is not supraglottic in origin and has invaded thyroid lamina at arrow.

representing the confluence of the vocal ligament, the thyroepiglottic ligament, the conus elasticus, and the internal perichondrium of the thyroid ala. This "tendon" is virtually avascular and offers a dense barrier to the spread of early glottic cancer.[8] Of the 20 specimens in which cancer has reached or crossed the anterior commissure at the level of the glottis, serial sections show that the adjacent thyroid cartilage has not been invaded in a single instance. Radiotherapy and conservation surgery are equally effective in treating T1b glottic cancer.[9]

In sharp contrast to the genuine T1b glottic lesion, those anterior glottic neoplasms that extend upward to attack the base of the epiglottis invade the thyroid cartilage in nearly every case. Such lesions are usually ulcerated and extensively infected. Of 26 such specimens in our laboratory, 19 showed invasion and destruction of the adjacent thyroid cartilage. Nine of the 26 specimens had been treated unsuccessfully by radiotherapy, and of these nine, six showed destruction of the adjoining framework. Of the remaining 17 untreated specimens, 13 showed a similar destruction of the adjacent framework.

An ominous feature of this type of anterior commissure cancer is its tendency to advance within the ossified lower edge of the thyroid lamina between intact layers of internal and external perichondrium. In so doing, cancer replaces the cancellous framework under normal soft tissue, often at some distance from visible tumor.[7] This type of spread within perichondrial layers has been observed only in those specimens in which cancer has destroyed the anterior thyroid cartilage as described above. This latter feature undoubtedly would be discovered at surgery, and would, in itself, disqualify the lesion for any procedure less than total laryngectomy.

SUBGLOTTIC SWELLING

Glottic cancer, having invaded the paraglottic space and produced fixation, may spread within this space under a largely intact subglottic mucosa. The most obvious clinical finding in this case may be an indurated swelling below the cord (or radiographic "shoulder"), with relatively little tumor visible by laryngoscopy. Biopsy of the swollen area often fails to obtain tumor that lies deep to the tough conus elasticus.

If such a swelling can be seen to extend 1 cm or more below the level of the glottis, the tumor, in escaping through the cricothyroid membrane, nearly always invades the lower, ossified edge of the thyroid ala, and often the upper edge of the cricoid. Surgical elevation of the external perichondrium of the thyroid ala in such a case risks exposing and disseminating cancer cells.[7]

SUPRAGLOTTIC SWELLING

Fullness and induration of the false cord in the absence of visible tumor can be a source of repeatedly negative biopsy reports. The swelling is usually due to one of two causes: 1) cancer in a laryngocele or 2) cancer invading the submucosal substance of the supraglottic larynx from a primary location in the pyriform sinus.

In the first instance, cancer arising on the superior surface of the true cord or in the depth of the ventricle may extend upward, displacing the overlying false cord toward the laryngeal lumen. This is most likely to occur in the presence of a preexisting laryngocele. Cancer in this case is not actually "submucosal," because both the superficial and deep surfaces of the false cord are usually free of cancer; nor is the substance of the false cord between these two layers involved with cancer (Fig 2). If repeated biopsies are directed to the supraglottic protuberance, they yield no cancer unless the false cord is first incised through its full thickness — both the laryngeal and ventricular surfaces — to gain access to the tumor in the ventricle (or laryngocele).

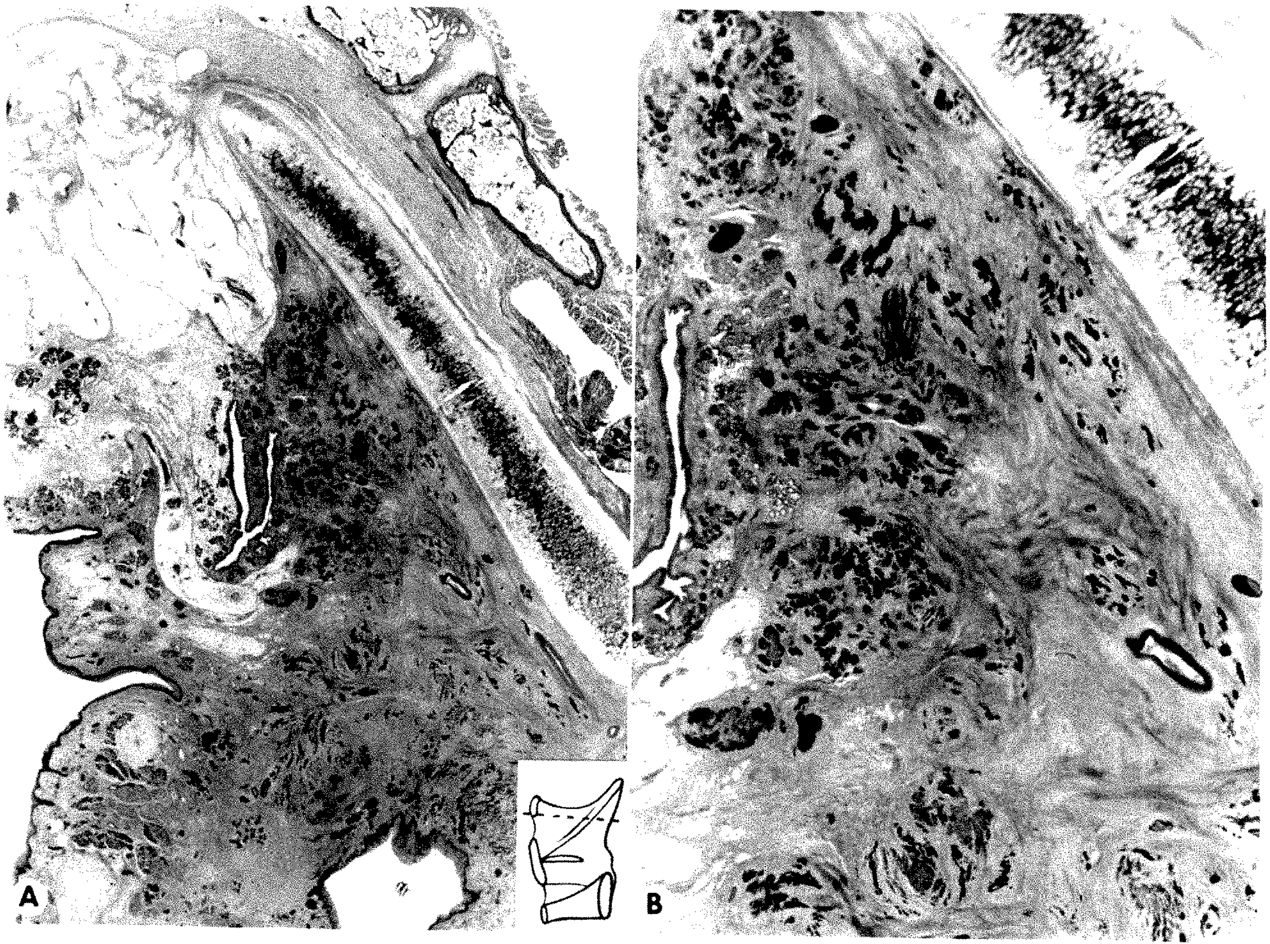

Fig 3. Transverse section of pyriform sinus cancer following radiotherapy. A) Nests of cancer cells lie deep below healed-over surface of supraglottic larynx. Biopsy of such areas usually fails to obtain evidence of cancer. B) Higher-power view of cancer shown in A.

In the second instance, pyriform sinus cancer may spread anteriorly and medially to invade the supraglottic tissues, displacing the false cord medially into the lumen without appearing on its surface. This type of cancer is often mistaken for a transglottic growth, particularly if the primary lesion in the pyriform sinus is small or otherwise difficult to identify.[10]

PREEPIGLOTTIC SPACE

Cancer of the infrahyoid portion of the epiglottis tends to spread anteriorly into the preepiglottic space, where it is not always detectable by radiographic techniques. Its presence in this space is important because of the poor blood supply that allows the large tumor to undergo central necrosis. This may explain its relative resistance to radiotherapy.[11]

HYOID BONE: TAKE IT OR LEAVE IT?

After invading the preepiglottic space, cancer is confined for a time by a fibroelastic membrane that gives to its advancing margin the appearance of a "pushing edge," almost as though it were encapsulated.[8] This feature of supraglottic cancer nearly always results in a tumor-free space between the hyoid bone and the advancing edge of tumor, allowing preservation of the hyoid at horizontal supraglottic laryngectomy. This technique assures a more secure reconstruction of the pharyngotomy and, in the opinion of many surgeons, an earlier rehabilitation of deglutition.[12] It is only the large, far-advanced lesion in the preepiglottic space that contacts the hyoid bone and requires its removal. This latter type of behavior has been found in only two of the 71 supraglottic lesions in our collection that were sectioned in a plane that would demonstrate involvement or noninvolvement of the hyoid. The need for hyoid resection can be determined before the bone is freed at operation, and is indicated by

INVASION OF FRAMEWORK BY CANCER IN 442 SPECIMENS

Location	*Total No.*	*No. Invaded*	*%*
Glottic	137	36	26
Transglottic	91	46	51
Supraglottic	112	0	0
Pyriform sinus	102	38	37

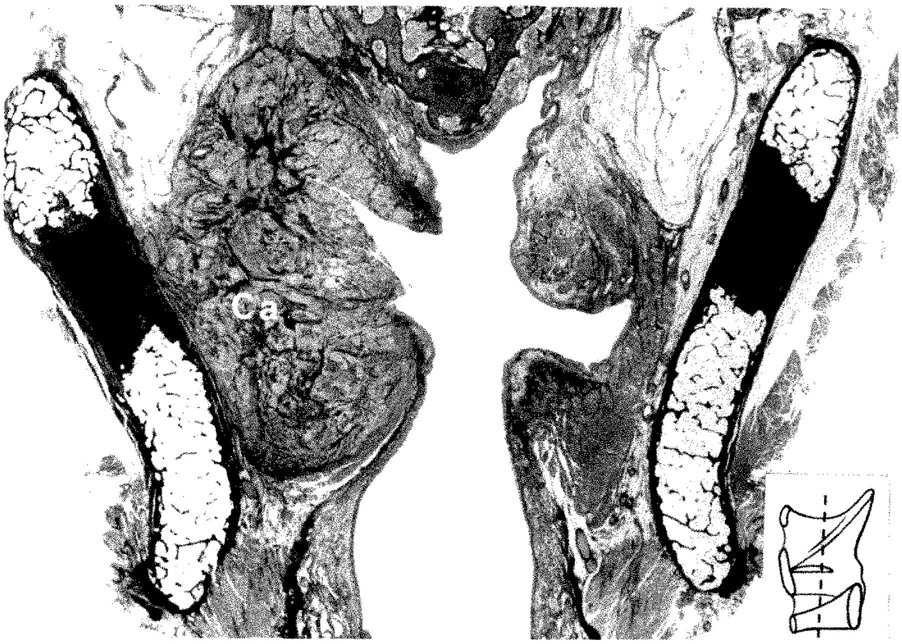

Fig 4. "Radiographic window" in coronal section of transglottic cancer within paraglottic space. Dark segment in each lamina is island of unossified cartilage, and these may simulate framework invasion by adjacent cancer (Ca).

induration or palpable tumor mass at the thyrohyoid membrane or vallecula.

REPEATEDLY NEGATIVE BIOPSY REPORTS

Apart from the absence of cancer and the failure to perform a biopsy on the tumor itself, repeatedly negative biopsy reports in the presence of cancer may occur under several conditions. The lesion may be difficult to expose for biopsy, as in the case of a small growth at the base of the epiglottis or at the anterior commissure. Other, less obvious reasons, however, may present problems.

When radiotherapy has been unsuccessful, the surface of the original tumor may have healed, leaving nests of viable cancer cells scattered within the deeper tissue (Fig 3). These cells are often difficult to obtain even with deep biopsy, and the procedure usually results in delayed healing and persistent, localized pain.

The depth of the laryngeal ventricle may be the site of primary cancer that then spreads superiorly and inferiorly under the intact surface of the true and false vocal cords to become "transglottic." Swelling of the ventricular band and true cord may be the only evidence of its presence. Angulated forceps are usually necessary in obtaining a specimen of cancer in this deep recess.

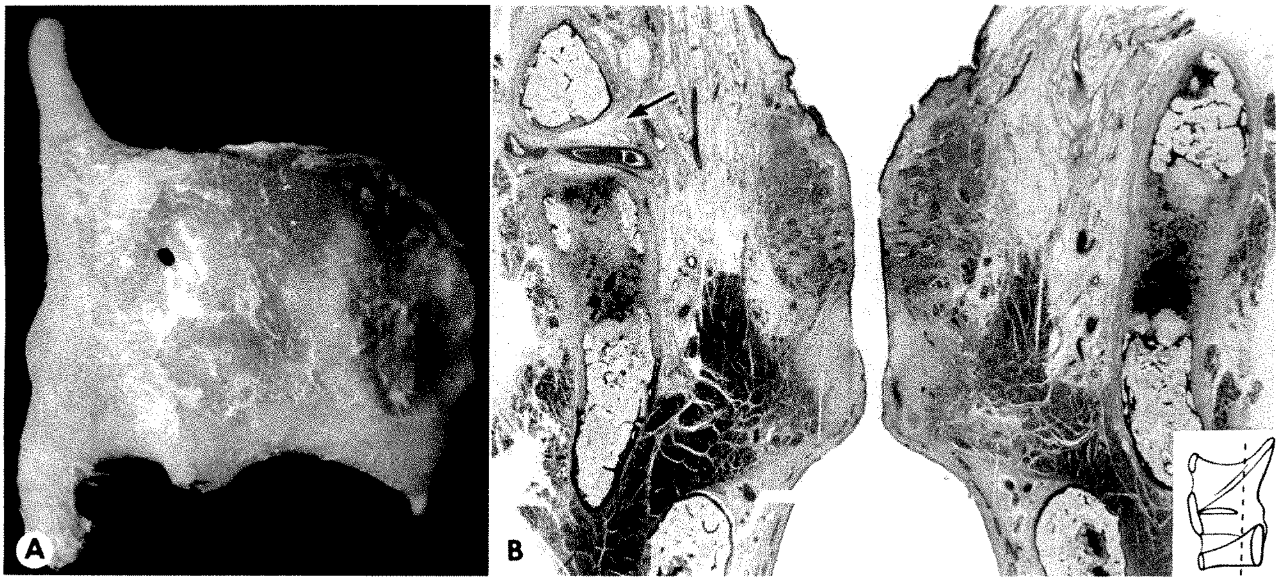

Fig 5. Anatomic foramen. A) At its usual location at base of greater cornu of thyroid ala. This opening should not be mistaken for framework invasion during horizontal supraglottic laryngectomy, but area should, if present, be taken for frozen section. B) Coronal section of anatomic foramen similar to that shown in A. This foramen is unilateral and transmits artery and vein (arrow). It is significant that even in specimens showing large supraglottic tumors adjacent to actual foramina, cancer had not extended through foramen.

RADIOGRAPHIC EVALUATION

A remarkable feature of supraglottic cancer is its failure to have invaded the thyroid lamina in a single instance among the 112 surgical specimens removed by total or partial laryngectomy and examined in whole organ sections. This statement applies to tumors whose lower edge has not crossed the ventricle or anterior commissure by inspection or radiography (see Table). Gross examination of the inferior extent of a lesion after pharyngotomy has been sufficient to define its limits of infiltration in our experience. This fact means that an area of radiolucency in the upper third or half of the thyroid ala observed in pretreatment radiographic imaging of a supraglottic cancer is not due to invasion by cancer if the lower edge of the lesion does not descend below the ventricle or the anterior commissure by clinical assessment. Such areas of radiolucency are due to variations in the patterns of ossification.

One such pattern is illustrated by the "radiographic window," consisting of an unossified area of cartilage within an otherwise ossified part of the thyroid lamina. Such unossified islands were found in 31 of the 121 coronally sectioned specimens (26%) when examined in serial section. They averaged 5 mm in diameter and could be mistaken on scanning studies for invasion of the framework by adjacent tumor (Fig 4).

Actual openings, or foramina, in the posterosuperior portion of the thyroid lamina were found in 47 of our 121 coronally sectioned specimens (39%) and in 39 of 69 cadaver specimens (57%). The openings are small, averaging 2.5 mm, and probably would be missed on radiographic examination. Since they are quite common, the laryngeal surgeon must not mistake them for framework invasion by supraglottic or pyriform sinus cancer. In addition, as such openings may transmit the superior laryngeal artery and a portion of the external branch of the superior laryngeal nerve (Fig 5), the contents of the foramina are better left undisturbed during surgery for benign lesions or functional disorders of the larynx.[13]

Supraglottic cancer's respect for the thyroid ala has an important surgical implication. It means that elevating the external perichondrium of the thyroid cartilage at horizontal supraglottic laryngectomy is relatively safe oncologically. If the surgeon discovers an area of soft tissue or tumor in the thyroid lamina while elevating the perichondrium, and frozen section shows cancer, the lesion is not "supraglottic," but transglottic. Careful inspection of the laryngectomy specimen in this case will show that the downward extent of the "supraglottic" tumor has been underestimated, and that the cancer has extended below the ventricle or anterior commissure.[11] Total laryngectomy is mandatory in this type of transglottic cancer.

IRRADIATION EFFECTS ON OSSIFIED CARTILAGE

Fifty serially sectioned laryngectomy specimens were studied to determine whether therapeutic external irradiation administered to the human larynx has selective effects on the osteoclast cell population and subsequent bone resorption. Irradiated and nonirradiated tissues were compared, as were cases with and without laryngeal framework involvement by cancer.

Morphometric studies indicated that framework invasion correlates significantly with both increased numbers of osteoclasts and increased bone resorption. This study also demonstrated that radiation therapy resulted in similarly increased osteoclast activity among cases without framework involvement by cancer. In these cases irradiation appeared to act independently of tumor in producing osteoclast activation.[14]

SUMMARY

Whole organ serial sections of laryngectomy specimens have shown that the spread of early cancer resembles the spread of fluids, dyes, and radioisotopes injected into various parts of the larynx by previous investigators. They have provided graphic evidence of the patterns by which cancer spreads from one part of the larynx and hypopharynx to another.

They also have demonstrated the fibroelastic membranes and ligaments that form the boundaries of intralaryngeal compartments within which cancer is confined in its early stages. They thus have added support to the concept of partial laryngectomy for selected lesions. Whole organ sections of laryngectomy specimens have allowed a more accurate interpretation of preoperative CT and MRI scanning and have provided additional help with clinical staging.

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The Casselberry Award was established to encourage the advancement of the art and science of laryngology and rhinology. The award is given for outstanding theses or accomplishments in laryngology and rhinology and consists of a suitable sum of money and a certificate from the Association. Competition for this award is limited to those persons whose abstracts are selected for consideration for inclusion in the annual scientific program. Abstract forms may be obtained from the Secretary, H. Bryan Neel, MD, 200 First Street SW, Rochester, MN 55905. Individuals wishing to compete for this award must submit an entry in the form of a complete thesis to Eugene N. Myers, MD, President, 230 Lothrop Street, Pittsburgh, PA 15213, no later than December 1, 1989. The candidates and theses will be reviewed by a committee. If a winner is selected, the Casselberry Award will be presented at the 111th annual scientific meeting, to be held at the Breakers Hotel in Palm Beach, Florida, April 28-29, 1990.

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PHONOSURGICAL STUDIES: FAT-GRAFT RECONSTRUCTION OF INJURED CANINE VOCAL CORDS

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Damage to the vocal cords can result in scarring and impaired vibration and can manifest clinically as hoarseness and loss of vocal power. If the vibratory characteristics could be restored in these scarred vocal cords, the vocal intensity and efficiency of phonation also should improve. In an effort to enhance the vibration of damaged vocal cords, we implanted a submucosal fat autograft within the injured vocal cord cover layer of dogs 6 weeks after unilateral mucosal excision had been performed. Three months postoperatively these animals were compared to normal dogs and those with mucosal excision but no fat-grafting. Acoustic and biomechanical measures of phonation were collected from an excised larynx preparation. We found that the fat-augmented vocal cords had lower threshold pressures for phonation, greater vocal intensity, and more efficient acoustic output than injured vocal cords without the fat-grafting. These results provide a foundation for further research on reconstructive surgery of damaged vocal cords.

KEY WORDS — fat graft, phonosurgery, vocal cord, vocal efficiency.

INTRODUCTION

Phonatory performance is sensitive to structural characteristics of the vocal cords. Damage to the laryngeal mucosa can result in scarring and impaired vibration and can manifest clinically as hoarseness and loss of vocal power. With our contemporary understanding of vocal cord structure and vibration,[1] investigation of vocal cord pathophysiology now has firm underpinnings.

Unique anatomic and biomechanical properties of the vocal cords have been shown to play a central role in normal phonatory activity. A series of studies by Hirano et al[2,3] and more recent theoretic work by Titze et al[4,5] have supported a body-cover theory of vocal cord structure and function. Basically this model presents the vocal cord as a layered system having a "cover" consisting of the surface epithelium and underlying superficial lamina propria, and a "body" comprising the deeper lamina propria and the vocalis muscle. The intermediate and deep parts of the lamina propria constitute a transition or coupling zone.[6] The viscoelastic properties of the vocal cords are being investigated.[7] It seems that the gelatinous, relatively compliant nature of the lamina propria is critical to normal vocal cord vibration. For example, the oscillation threshold pressure is related to a number of factors, including tissue viscosity, vocal cord thickness, and mucosal tissue stiffness.[5]

The vibratory behavior of the cover layer can be altered readily by various physical insults. Such disturbances include tissue edema, mass lesions, and the sequelae of surgery or trauma. Postsurgical scarring of vocal cords can be particularly troubling clinically, since further conventional surgical intervention stands to worsen any scarring. The resultant stiffening in the lamina propria would be expected to alter phonation by impairing movement of the mucosal cover.

Animal studies have demonstrated chronic fibrotic changes in vocal cords subsequent to operative stripping of the superficial mucosa. In a study of 12 cats, Leonard et al[8] documented by histology increased fibrous elements after vocal cord stripping. Reepithelialization occurred in the early weeks postoperatively, and often no evidence of mucosal disease was present by gross inspection alone. Since no physiologic examinations were performed, the correlation of structural damage to phonatory impairment could not be addressed.

In an effort to improve vocal cord wound healing, Okamura et al[9] used a mucosal graft to cover vocal cords after mucosal excision. They reported that the mucosal graft resulted in a faster healing process with less scarring and a relative preservation of function. The mucosal graft itself did not remain viable. Rather, it was purported to serve as a temporary protective layer that improved healing. While such a procedure is potentially of clinical value in the setting of certain acute laryngeal injuries, operative rehabilitation of the scarred vocal cord remains a difficult problem.

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The purpose of this study was to investigate the effects of a vocal cord augmentation procedure on phonation in scarred canine vocal cords. If the vibratory characteristics could be restored in these damaged vocal cords, then sound intensity and vocal efficiency also should be improved. Whereas submucosal injections of Teflon and other materials have been used routinely in phonosurgery solely to medialize the paralyzed vocal cord, for the present study a lighter and more compliant material was sought to enhance vibration of the damaged cover layer. A submucosal fat autograft was considered as one such possibility. Fat is a readily available, compliant, nonreactive biomaterial with relatively low metabolic requirements. Although the viscoelastic properties of fat have not been measured, it was expected to be more compliant than scar tissue or injectable Teflon, and thus more conducive to vocal cord vibration.

METHODS

Animals. Thirteen adult female conditioned laboratory dogs were used in this study. Body weights were 15 to 20 kg.

Operative Procedures. Four animals had no operative procedures and served as the unoperated control group, hereafter referred to as the normal group. Nine animals underwent a right true vocal cord mucosal excision under short-acting general anesthesia of ketamine/xylazine (Rompun) in a 75% to 25% ratio, 4- to 6-mL intramuscular injection. The mucosal excision was carried out endoscopically with use of standard suspension laryngoscopy techniques and an operating microscope. Attention was given to preservation of the anterior commissure region. The excisions were directed along the leading vocal cord edge, at a depth to include upper-to-middle lamina propria. The vocalis muscle was not violated. Four animals had no further operative intervention and constitute the nonreconstructed control group, hereafter called the mucosal excision group.

After at least 6 weeks' healing from the mucosal excision, five animals underwent a fat-autograft right vocal cord augmentation operation. This group will be referred to as the fat-graft group. With use of general anesthetic as described above, a low tracheotomy was performed and a small quantity of abdominal subcutaneous fat was harvested and rinsed thoroughly in saline. A midline laryngofissure approach to the endolarynx was performed. A McCabe flap elevator was introduced through a small incision just inferior and posterior to the anterior commissure on the right side and was used to create a tunnel under the leading vocal cord edge. Into this pocket a pad of fat (water volume displacement ranged from 0.2 to 0.4 mL) was placed. The anterior entrance to the tunnel then was closed with a 5-0 chromic purse-string suture. The laryngofissure and cervical flaps were closed in layers with Vicryl sutures. The temporary tracheotomy was stented open with Vicryl sutures, but no tracheotomy tube was used postoperatively. Perioperatively, 4 mL of penicillin suspension was given intramuscularly (penicillin G 150,000 U/mL and benzathine penicillin 150,000 U/mL). All animals recovered uneventfully and a 2-month healing period ensued before the animals were killed painlessly.

Excised Larynx Preparation. Larynges were obtained immediately after the animals were killed by an intracardiac injection of T-61 euthanasia solution. The larynges were bathed in D5 lactated Ringer's solution until the in vitro phonation studies were carried out.

The excised larynx phonation instrumentation is based on the methods of Baer[10] and has been documented in detail.[11] A humidified air column with regulated flow provides a subglottic airstream while concomitant pressure is monitored directly from a water-filled manometer U-tube. A video camera was set in a line directly above the larynx and a strobe light was directed in from the side. A microphone and a sound pressure level (SPL) meter were mounted at 20 cm from the glottis and oriented at 45° to the glottic plane. Normal saline was applied to the vocal cords periodically to prevent dessication. Sequential pressures, flows, and SPLs (in decibels) were recorded, along with videostroboscopic and acoustic waveform data.

Histology. After the phonation studies the larynges were placed in formalin and processed for histology. The tissues were decalcified, embedded in celloidin, and cut in 20-μm sections. Hematoxylin and eosin stains were applied.

Data Analysis. Data were summarized into mean ± standard error of the mean (SEM) for graphic comparisons.

Analysis of variance was used for all statistical analysis, and significance was set at the $p<.05$ level.

Calculation of glottal efficiency was based on the ratio of radiated acoustic power to aerodynamic (subglottic) power. In accordance with Schutte[12] and Titze,[13] acoustic power (pascals [Pa]) was determined by the equation

$$Pa = 4\pi r^2 I$$

where I equals SPL in watts per square meter and r equals distance to the microphone in meters. Sound pressure level was expressed in watts per square meter by the following conversion.

$$SPL = 10^{\text{No. of dB}/10} \times 10^{-12}\ W/m^2$$

Subglottic power was found by multiplying flow in milliters per second by the subglottic pressure in kilopascals (1 cm water pressure = 98 Pa).

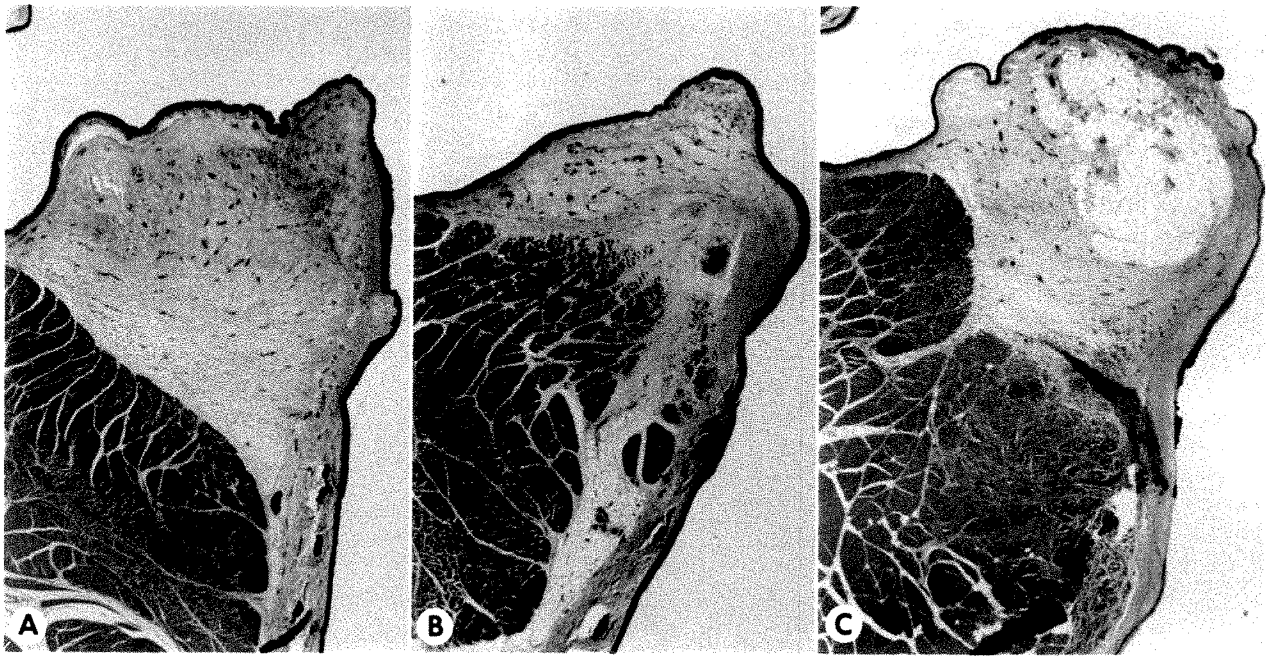

Fig 1. Cross-section photomicrographs through canine vocal cords (H & E). A) Unoperated vocal cord showing mucosal cover and underlying muscle, which constitutes body. B) Vocal cord approximately 2 months after partial-thickness mucosal excision. Surface has reepithelialized, but loss of tissue from mucosal cover remains apparent. C) Vocal cord approximately 2 months after fat-graft implantation of injured vocal cord. Fat implant is localized near leading edge of vocal cord.

RESULTS

Histology. In four of the five fat-grafted animals the submucosal pocket of fat could be identified clearly. The fat was localized discretely and typical fatty architecture was evident. In one fat-grafted animal a discrete fat pad was not found. There was no fat present in the leading-edge region of normal animals or mucosal excision animals. In the mucosal excision animals, reepithelialization occurred, but a deficiency of lamina propria mass was noted. Representative photomicrographs are shown in Fig 1.

Threshold Pressure of Phonation. Normal canine larynges had a mean oscillation threshold pressure of 7.2±0.7 cm H_2O (mean±SEM). The data for normal animals were consistent with previous excised larynx phonation data.[14] Animals having mucosal excision without fat-graft augmentation had a significantly elevated threshold pressure of 20.2±2.7 cm H_2O ($p < .01$). Larynges with fat-graft augmentation had a mean threshold of 9.8±1.8 cm H_2O. This was significantly less than the excision-only group ($p < .01$), but was not significantly different from the normal group. These results are summarized in Fig 2.

Sound Intensity. Phonatory intensity was measured as absolute SPL in decibels. Mean SPLs were compared across animals at a 32-cm H_2O driving (subglottic) pressure. At this approximately mid-range reference pressure, normal larynges produced a mean intensity of 87.9±0.4 dB. For animals in the mucosal excision group, the mean was lowered significantly, to 82.0±1.6 dB ($p < .01$). Fat-grafted larynges phonated at 85.7±1.1 dB, which was significantly higher than the level in the mucosal excision-only group ($p < .05$), but not different than that in the normal animals. The results are shown in Fig 3.

Glottal Efficiency. Glottal efficiency relates emitted acoustic power to the pneumatic driving (subglottic) power. Mean efficiency for the normal larynges was $5.95 \pm 0.34 \times 10^{-5}$, (ie, 0.00593%). Mean efficiency was reduced significantly in the mucosal excision group, to $1.63 \pm 0.76 \times 10^{-5}$ (0.00163%) ($p < .01$). The efficiency also was reduced in the fat-graft group, to $3.62 \pm 0.43 \times 10^{-5}$ (0.00362%) ($p < .05$), but the value was still significantly higher than the mucosal excision group mean ($p < .05$). These data are summarized in Fig 4.

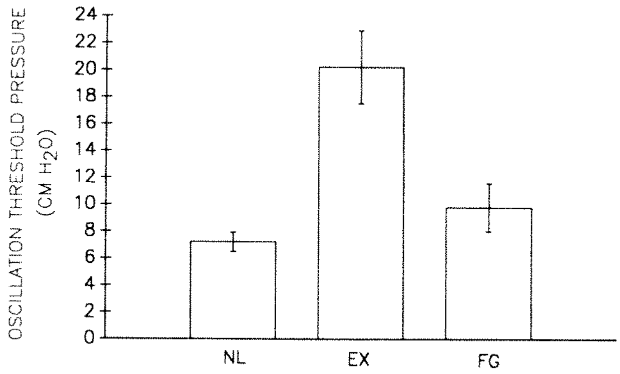

Fig 2. Mean threshold pressure for vocal cord oscillation. NL — normal, unoperated animals, EX — mucosal excision only, FG — mucosal excision followed by fat-graft reconstruction. Error bars indicate standard error of mean.

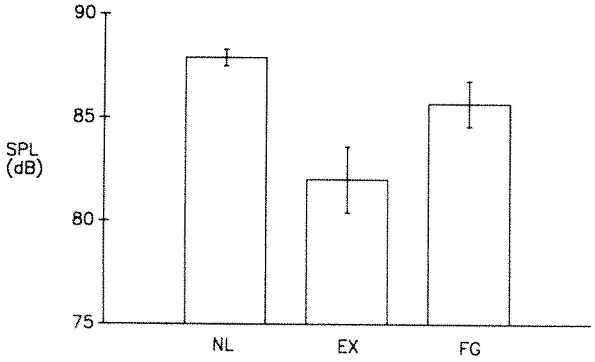

Fig 3. Mean phonatory intensity at 32 cm H2O driving (subglottic) pressure. SPL — sound pressure level in decibels. Other abbreviations and symbols as in Fig 2.

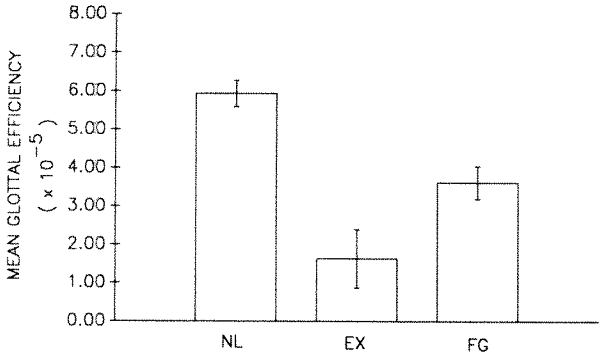

Fig 4. Mean glottal efficiency of phonation. Abbreviations and symbols as in Fig 2.

Vocal Cord Vibration. Videostroboscopic recordings of phonation were reviewed for qualitative features and direct amplitude measurements. Normal canine vocal cords had approximately symmetric vocal cord excursion with maximal amplitude in the middle third region. There was no gross phase asymmetry.

After mucosal excision, phonatory wave motion was altered. In general, amplitude was lower in the damaged vocal cord relative to the unoperated side. In some cases the operated vocal cord would demonstrate polymodal vibration along its length and would be out of phase with the opposite, unoperated vocal cord. Although some fat-graft animals had similar disturbances of vibration, the amplitudes were improved toward normal. There was considerable variability among the individual animals.

All fat-grafted larynges were capable of bilateral vocal cord oscillation with periodic vibration. One of the mucosal excision–only animals was incapable of producing sustained periodic vibration and thus could not be included in the following amplitude measurements. Amplitude measurements revealed no significant difference in mean amplitude between left and right vocal cords in the normal animals. In contrast, the mucosal excision animals had decreased amplitude in the injured vocal cord. In order to compare amplitudes across treatment groups for various phonation pressures, measurements of vocal cord amplitude were analyzed with use of analysis of variance with repeated measures. The data are plotted in Fig 5. Mucosal excision animals had diminished amplitude compared to the normal group ($p < .05$). The mean amplitudes for the fat-graft group are not significantly different in amplitude from the normal group, but the variability is much greater. Despite the partial overlap of data for individual animals, the fat-graft group had improved vibratory amplitudes on the average, compared to the mucosal excision group ($p < .05$).

It should be noted that there were no significant differences in mean vocal cord length between groups: normal, 15.9±0.7 mm; mucosal excision, 16.0±0.8 mm; and fat-graft, 15.1±1.4 mm.

DISCUSSION

Few investigators have addressed surgical management of chronically damaged vocal cords. Such cord injury might occur from trauma, certain chronic infections, or various laryngeal operations. One possible method for reconstructing a scarred vocal cord would be to replace the cover with a local flap of healthy mucosa. In 1959 Conley[15] reported phonatory improvements in partial laryngectomy patients who underwent local mucosal flap repair of laryngeal mucosal defects. The original rationale for repair with local mucosal flaps was to reduce the area of scarring and diminish the chance of stenosis. However, it is not clear whether a flap repair can be used to reconstruct a scarred vocal cord. Our experience with a single animal repaired by a local mucosal flap was that the larynx had a poor phonatory result. This was due most likely to the scarring that occurred as the flap healed in its new position.

Bouchayer and Cornut[16] have described an endoscopic treatment for vocal cord scarring. They re-

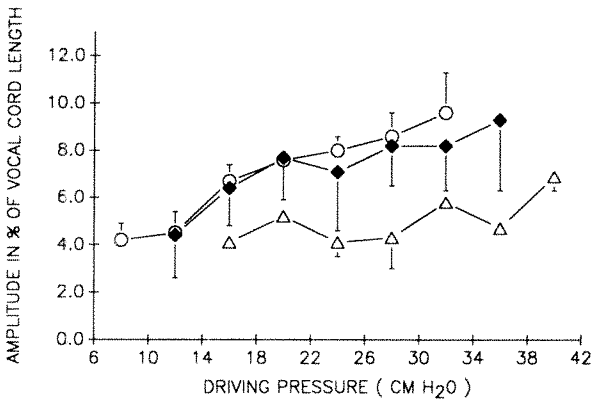

Fig 5. Mean amplitude of vocal cord vibration. Numbers are normalized to percentage of vocal cord length and represent means for right vocal cord (side of operative procedures, if any). For clarity, error bars are shown only on one side of each mean. Open circle — normal group, open triangle — mucosal excision only, filled diamond — fat-graft implantation after mucosal injury.

port that simple release of scarred mucosa by undermining, together with steroid injection, improves vocal quality and vibratory pattern. However, more information regarding length of follow-up and objective assessments will be needed before firm conclusions on this approach can be reached.

Dedo and Rowe[17] briefly mentioned their clinical experience with fat-autograft insertion to augment thin, scarred, bandlike cords, creating what they refer to as a pseudocord. Apparently they have had some success with this method, although occasional additional procedures were necessary to maintain or upgrade the improvements. Our procedure was similar to that described by Dedo and Rowe, and the excised larynx preparation allowed us to assess quantitatively the effects of fat-grafting.

Excision of the vocal cord mucosa produced structural changes associated with decrements in phonatory measures and amplitude of vibration. We found that damaged vocal tissues required higher driving pressures to initiate phonation and used more energy to maintain it. The findings of increased threshold pressure of phonation, together with reduced glottic efficiency and diminished wave amplitude, are consistent with our intuitive expectations for damaged, scarred vocal cords. The fat-graft submucosal augmentation procedure introduced in this study resulted in significant improvements in these measures of function.

It is well known that compliance (and its inverse, stiffness) is a determinant of vibration in mechanical and acoustic oscillating systems.[18] The primary effect we desired to achieve by fat-graft implantation was an increase in vocal cord compliance. After fat-grafting, overall stiffness in the cover layer should be reduced and amplitude of vibration should increase toward normal. Our data support this hypothesis, but direct confirmation of tissue properties would be desirable. Other effects of the graft, including volume enhancement and change in vocal cord mass, also could contribute to the observed results.

In a theoretic study of small-amplitude vocal cord oscillations, Titze[5] noted that the threshold pressure is reduced by factors such as decreased tissue damping, decreased stiffness, increased vocal cord thickness, and decreased glottal width (separation between the cords). Since each of these parameters can be affected by a submucosal fat graft, it is difficult to isolate the specific manner by which the graft exerted its effect. Better separation of these effects would seem desirable because it has bearing on how much fat should be inserted and whether other biomaterials might be suitable for this type of operation. It should be noted that partial fat atrophy was anticipated, so the fat implant seemed excessive in volume at the time of operation. This excess of bulk had resolved by the time of the phonation studies.

Correlation of histology and phonation data suggests that position of the fat graft is important. The two larynges with greatest efficiency and amplitude of vibration had the fat graft situated in the leading-edge region. In contrast, an animal with the fat more laterally placed had poorer phonation measures. The single animal in which presence of the fat graft could not be confirmed histologically had decreased vibration amplitude and less than average glottal efficiency.

In summary, fat-graft augmentation in damaged canine vocal cords resulted in improved amplitude of vibration, improved phonatory intensity, greater efficiency, and decreased phonation pressure thresholds. These encouraging results provide a foundation for further research on reconstructive surgery of damaged vocal cords.

ACKNOWLEDGMENTS — The authors thank the following individuals: Dr Adrienne Perlman for her helpful discussions and encouragement; Dr Paul Cooper for veterinary support; David Drucker, Penny Harding, and Ray Allen for their excellent technical support; Pat Wehrle and Kay Joslyn for providing materials; and Brenda Booth, Dr Rachel Kleiman-Wexler, and Dr Randy Prince for their help with the graphics and statistics.

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The University of Iowa Department of Otolaryngology–Head and Neck Surgery and the International Cochlear Implant Association will hold the Second International Cochlear Implant Symposium in Iowa City on June 4-9, 1990. The symposium will focus on basic science aspects of electrical stimulation on the auditory system, new cochlear implant strategies, clinical application in both adults and children, and rehabilitation and educational issues. Please submit abstracts to Bruce J. Gantz, MD, Department of Otolaryngology–Head and Neck Surgery, University of Iowa Hospitals and Clinics, Iowa City, IA 52242.

Ann Otol Rhinol Laryngol 98:1989

LONG-TERM RESULTS OF NERVE-MUSCLE PEDICLE REINNERVATION FOR LARYNGEAL PARALYSIS

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CLEVELAND, OHIO

Between 1976 and 1986, 214 patients with bilateral vocal fold paralysis and 73 patients with unilateral vocal fold paralysis were managed by the author using the nerve-muscle pedicle technique for reinnervation. Follow-up of at least 2 years has been obtained on 202 of the bilaterally and 70 of the unilaterally involved patients. Long-term success has been achieved in 74% of the bilateral group and 88% of the unilateral group. Successful reinnervation of unilateral paralyses usually maintains voice correction indefinitely, but there is late (2 to 5 years postsurgery) deterioration of successful airway restoration in approximately 17% of bilateral cases, which appears to be due to development of cricoarytenoid arthritis.

KEY WORDS — laryngeal paralysis, laryngeal reinnervation, nerve-muscle pedicle.

INTRODUCTION

In 1976 and 1977, the author reported the use of nerve-muscle pedicle reinnervation for patients with bilateral vocal fold paralysis[1] and for selected patients with unilateral paralysis.[2] Since that time, 214 patients with bilateral paralysis and 73 with unilateral paralysis have been managed with these techniques and have been followed for at least 2 years. Long-term results are presented and analyzed in this report.

MATERIALS AND METHODS

Three hundred ninety-four patients with bilateral vocal fold immobility were seen by the author at The Cleveland Clinic Foundation between January 1976 and December 1986. Of these, 214 (54.3%) were found to be suitable candidates for attempted vocal fold reinnervation using the nerve-muscle pedicle technique. Any patient with bilateral fixation confirmed by arytenoid palpation with use of paralytic anesthesia[3] and/or, in occasional cases, whose previous neck surgery or disease rendered the necessary branches to the ansa hypoglossi nerve unavailable were rejected for this approach to restoration of airway. Length of time that the paralysis had been present was not, per se, a criterion for rejection, although the incidence of fixation of the cricoarytenoid joint increased with time.[4]

Tracheotomy was performed at the time of reinnervation in those patients who had not already had one (103 of 214 or 48%). Nerve-muscle pedicle reinnervation was carried out via neck incision on the side of greater mobility, or on the left side when there was equal passive mobility of both cricoarytenoid joints. The technique used has been described in detail elsewhere.[5,6] Patients were discharged within 48 hours with rare exceptions and were followed bimonthly if they lived close enough to Cleveland, and at greater intervals or by referring otolaryngologists when they lived at greater distances. The procedure was considered a success when the patient could be decannulated with airway capability that was improved from the preoperative state and sufficient to permit reasonable day-to-day activity without significant limitation or airway restriction during subsequent upper respiratory tract infections or allergic diathesis. All patients in this study were followed at least 2 years from the time of surgery.

Six hundred forty-three patients were seen during the same 10-year period with unilateral vocal fold immobility. Of these, 73 (11.3%) were subjected to nerve-muscle pedicle reinnervation in an attempt to restore phonatory capability. Because the majority of patients with unilateral vocal fold paralyses recover or compensate spontaneously within 1 year of onset, and because Teflon injection remains the procedure of choice for those who do not achieve a satisfactory voice without intervention, only patients with voices that were critical to their livelihood or psychologic well-being were selected for unilateral reinnervation. Voice recordings were obtained preoperatively for comparison to serial recordings at intervals after surgery.

The technique used for unilateral reinnervation is described elsewhere.[6,7] Patients were discharged in 24 hours and were evaluated bimonthly either by the author and a senior speech and language pathologist when proximity permitted, or by the referring otolaryngologist and through high-quality tape recordings when patients lived at great distances. Voice results were graded subjectively at 1 year by the surgeon, speech pathologist, and the patient as normal, greatly improved, somewhat improved, or

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From the Department of Otolaryngology and Communicative Disorders, The Cleveland Clinic Foundation.

Presented at the meeting of the American Laryngological Association, San Francisco, April 1-2, 1989.

REPRINTS — Harvey M. Tucker, MD, Dept of Otolaryngology and Communicative Disorders, The Cleveland Clinic Foundation, 9500 Euclid Ave, Desk A-71, Cleveland, OH 44195.

VOICE RESULTS AFTER UNILATERAL VOCAL FOLD REINNERVATION

	Normal	Greatly Improved	Somewhat Improved	Not Improved	Total
No. of patients	18 (25%)	42 (58%)	4 (5%)	9 (12%)	73 (100%)

not improved (see Table). All patients were followed for at least 2 years.

RESULTS

Bilateral Paralysis. Two hundred two of the 214 patients managed with the nerve-muscle pedicle technique for restoration of the airway were available for follow-up for at least 2 years after the procedure. Within 6 months or less of surgery, 180 (89%) met the criteria for successful decannulation with adequate exercise tolerance. There were only four complications in this group of patients other than failure to achieve successful reinnervation: three wound infections, all of which responded to antibiotic management, and one death due to exsanguinating hemorrhage from a tracheostomy site placed several months before at another institution.

Within a period varying from 2 to 5 years after nerve-muscle pedicle reinnervation, 31 of the 180 initially successful patients gradually redeveloped airway restriction that was of sufficient severity to require further intervention (usually reopening of the previous tracheotomy). Eighteen of them could be evaluated endoscopically under paralytic anesthesia by the author. In 16 of these 18 cases, cricoarytenoid fixation or ankylosis was identified. Thus, deterioration of the airway reduced the long-term success rate to 74% (149/202).

Unilateral Paralysis. Within 2 to 6 months after reinnervation for unilateral paralysis, 64 of the 73 operations were judged successful on the basis of marked voice improvement accompanying observable ability to adduct the previously paralyzed vocal fold and to tense it during elevation of pitch. There were no complications of surgery. Voice results improved for several months after initial success, especially if speech therapy was continued. After 1 year no further improvement of voice was recorded. Initial success of unilateral vocal fold reinnervation was, therefore, 88%. Subsequent persistent deterioration of voice occurred in only one of these initially successful cases and remains unexplained.

DISCUSSION

Late failures after initially successful reinnervation for bilateral paralysis seem to be related to development of ankylosis of the cricoarytenoid joint. Almost all of these occurred in older patients (>65 years old). It also appears that if airway improvement is maintained beyond 5 years of initial success that it will be permanent, although the number of patients involved and length of follow-up do not yet permit firm statistical conclusions.

The principle of nerve-muscle pedicle reinnervation has been reconfirmed in several laboratories,[8,9] but clinical success has not been widespread. Although the long-term results reported here should support this technique as a good way to manage bilateral vocal fold paralysis, it is clear that no procedure can be very useful if it cannot be performed reliably by most properly trained surgeons.

On the other hand, although the experience of other surgeons is limited, reinnervation for unilateral paralysis has worked so well that it should be considered seriously for best management of those patients whose voice remains unsatisfactory 1 year after onset of paralysis and who require a voice that is more than just "adequate." Teflon injection remains the procedure of choice for most patients because it is inexpensive and gives almost immediate improvement, and its results are generally good. Unlike reinnervation, however, it does not restore tensioning capability, and therefore pitch control remains poor.

CONCLUSIONS

Long-term results for nerve-muscle pedicle reinnervation of laryngeal paralyses demonstrate high initial success rates for both unilateral and bilateral cases. There is deterioration of initial airway improvement after 2 to 5 years in 17% of bilateral paralysis patients, but voice improvement achieved in patients with unilateral paralysis is well maintained. These procedures have been useful and reliable in managing selected patients with unrecovered vocal fold paralysis for over 10 years and therefore can be recommended for inclusion into the armamentarium of other surgeons.

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Ann Otol Rhinol Laryngol 98:1989

LARYNGEAL BRAIN STEM EVOKED RESPONSE

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WASHINGTON, DC

Sensory stimuli to the larynx evoke a laryngeal adductor reflex mediated by the brain stem via superior and recurrent laryngeal nerves. Aberrant laryngeal reflexes have been proposed to explain a number of poorly understood disorders, including "reflex apnea," idiopathic laryngospasm, and sudden infant death syndrome. The purpose of the present study was to evaluate far field brain stem recordings following stimulation of the superior laryngeal nerve to determine whether laryngeal brain stem response is a valid measure of laryngeal activity at the brain stem level. The nerve was stimulated electrically in adult cats, and the resultant laryngeal adductor response as well as far field brain stem activity was recorded. For the latter, six reproducible positive and five reproducible negative waves were obtained via posterior pharyngeal (+) and posterior cervical (−) recording electrodes. Response threshold and latencies were measured and evaluated as a function of stimulus parameters. Wave latencies corresponded closely to those reported in prior near and far field evoked response recordings.

KEY WORDS — brain stem, larynx, superior laryngeal nerve.

INTRODUCTION

Basic laryngeal reflexes are necessary for pulmonary protection. Aberrant or absent reflexes may cause laryngeal and/or pulmonary dysfunction. There are a number of conditions of unknown cause that may be linked to abnormal laryngeal function, including idiopathic laryngospasm, gastroesophageal reflux–related apnea or laryngospasm, spastic dysphonia, apnea of infancy, and sudden infant death syndrome.[1-3] Any of these disorders can result in life-threatening upper airway obstruction or apnea; however, without knowledge of underlying pathophysiology, appropriate treatment or cure is impossible.

Reflex glottic closure evoked by stimulation of the superior laryngeal nerve (SLN) has been well described. Sasaki and Suzuki[4] and Suzuki and Sasaki[5,6] have reported a short latency laryngeal adductor reflex response (LAR) in both animals and humans, produced by stimulating the SLN and recording impulses from the ipsilateral or contralateral recurrent laryngeal nerve (RLN). The proposed reflex pathway consists of SLN stimulation followed by vagal afferents carrying the stimulus through the nodose ganglion to the brain stem (nucleus solitarius). Laryngeal adductor motor neurons then are stimulated, probably in the nucleus ambiguus and reticular formation, resulting in vocal cord adduction and pulmonary protection (Fig 1).[1,7,8] Definition of anatomic or electrophysiologic abnormalities in this pathway may help explain the pathophysiology of laryngeal dysfunction and therefore facilitate treatment.

Auditory brain stem evoked response (ABR) testing has become an invaluable clinical method of studying central pathways of the eighth cranial nerve. Metson[9] has measured antidromic evoked potentials in an attempt to evaluate central pathways of the seventh cranial nerve in the cat, and Leandri et al[10] have evaluated brain stem evoked potentials after stimulation of the fifth cranial nerve in humans. Horseradish peroxidase studies have confirmed anatomically both peripheral and central components of the pathway of the tenth cranial nerve.[11,12] Although the peripheral laryngeal adductor reflex has been well studied electrophysiologically, the polysynaptic central pathway has not received the same attention until recently.

In 1987, Isogai et al[13] described a method in which averaged electrical activity was recorded simultaneously from the RLN and brain stem following electrical stimulation of the SLN in paralyzed cats. They termed the far field brain stem activity the laryngeal brain stem response (LBR). Four positive and four negative waves with reproducible latencies were described, and generator sources postulated.

The purpose of the present study was to reproduce as well as to further characterize these laryngeal evoked potentials by studying far field recordings of brain stem activity evoked by stimulation of the SLN in paralyzed and unparalyzed cats. The effects of stimulus parameters on latency, amplitude, and threshold data were evaluated as a preliminary step to defining optimal stimulus and recording parameters.

METHODS

Nine adult cats (1.8 to 2.5 kg) were premedicated with intramuscular ketamine hydrochloride (11

From the Department of Otolaryngology, Stanford University Medical Center, Stanford, California. Supported by a grant from the Katharine McCormick Foundation. This study was performed in accordance with the PHS Policy on Humane Care and Use of Laboratory Animals, the NIH *Guide for the Care and Use of Laboratory Animals*, and the Animal Welfare Act (7 U.S.C. et seq.); the animal use protocol was approved by the Institutional Animal Care and Use Committee (IACUC) of Stanford University. Dr Anonsen is now with the Bellevue Ear, Nose and Throat Clinic, Inc, PS, 1201 116th Ave NE, Bellevue, WA 98004.

Presented at the meeting of the American Laryngological Association, San Francisco, April 1-2, 1989.

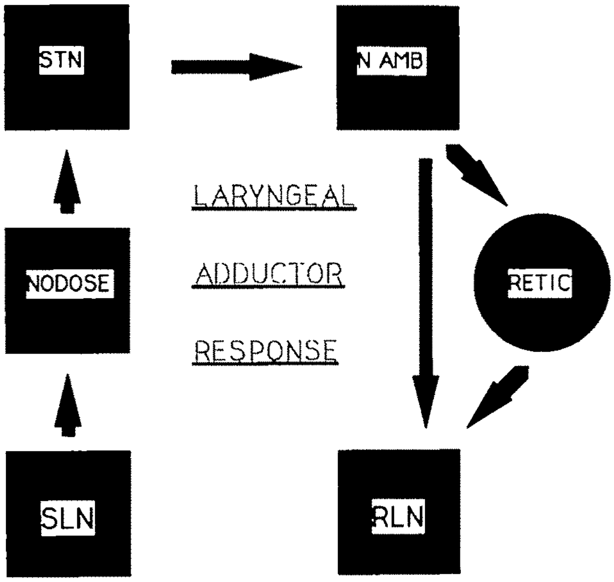

Fig 1. Proposed pathway of laryngeal adductor response. Stimulation of superior laryngeal nerve (SLN) results in excitation of vagal afferents that carry signal through nodose ganglion to nucleus solitarius (STN). Laryngeal motor neurons in nucleus ambiguus (N AMB) as well as neurons in reticular formation (RETIC) are stimulated to produce glottic closure via recurrent laryngeal nerve (RLN).

mg/kg) and xylazine (0.5 mg/kg). Anesthesia was maintained with intravenous ketamine HCl (11 mg/kg) and xylazine (0.5 mg/kg). Electrocardiogram and respiration were recorded simultaneously on a Grass polygraph (model 7E). Temperature was monitored continuously via a rectal probe and maintained within physiologic limits with a heating pad.

The anterior larynx and trachea were exposed through a midline vertical neck incision. A low tracheotomy was performed. The right SLN and RLN were exposed and bathed in mineral oil to prevent drying. A pair of insulated stainless steel stimulating electrodes (75 μm) were applied to the internal branch of the SLN just distal to its bifurcation into internal and external branches. A pair of insulated stainless steel hook electrodes (75 μm) were placed on the RLN 1 cm proximal to its insertion into the cricothyroid membrane to allow recording of the response evoked in the RLN by SLN stimulation, which is the LAR. The RLN was transected distal to the electrode placement to eliminate electrical activity through Galen's anastomosis. An insulated stainless steel hook electrode (175 μm) was placed through the soft palate into the posterior pharyngeal wall just inferior to the level of the hard palate (pharyngeal, noninverting or active lead) to record the LBR. Surface electrodes were applied to posterior cervical skin approximately at the level of the third cervical vertebra (C-3, inverting or reference lead) and to lateral neck skin (ground). In this manner, integrity of the LAR and adequacy of stimulus could be verified. In addition, timing of the LBR could be compared to that of the RLN response (Fig 2). Alternate surface electrodes were used in some animals to provide different recording montages. These included vertex (Cz) and forepaw electrodes.

The animals were paralyzed with intravenous pancuronium bromide (0.1 mg/kg) to eliminate the effect of muscle artifact on LBR recordings. Re-

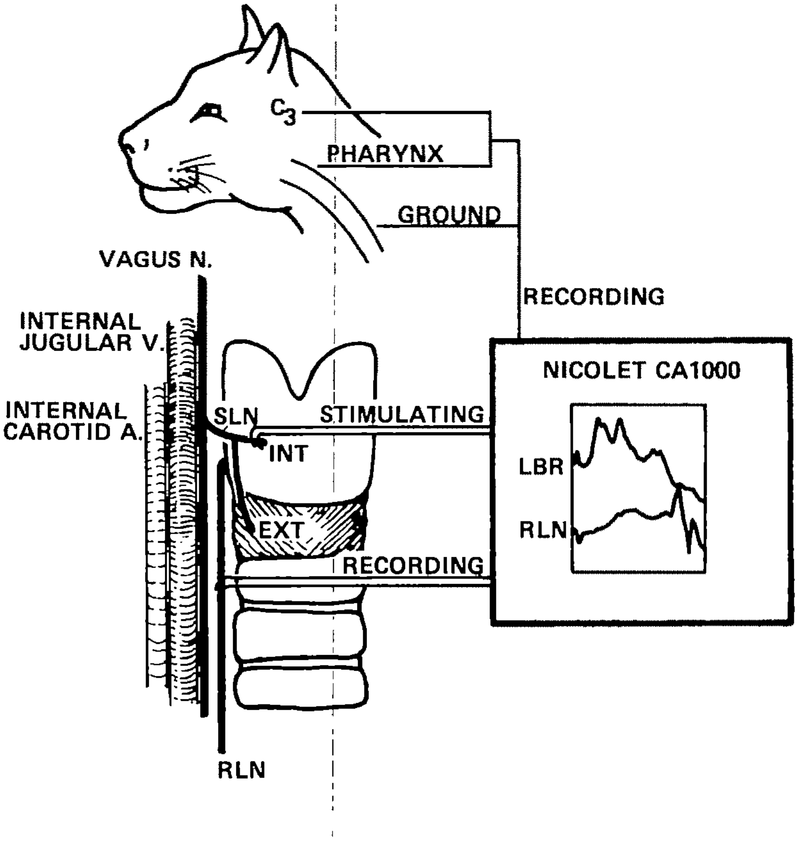

Fig 2. Experimental setup. Superior laryngeal nerve (SLN) was stimulated, and simultaneous recording of laryngeal brain stem evoked response (LBR) and laryngeal adductor or recurrent laryngeal nerve (RLN) response was plotted (see text).

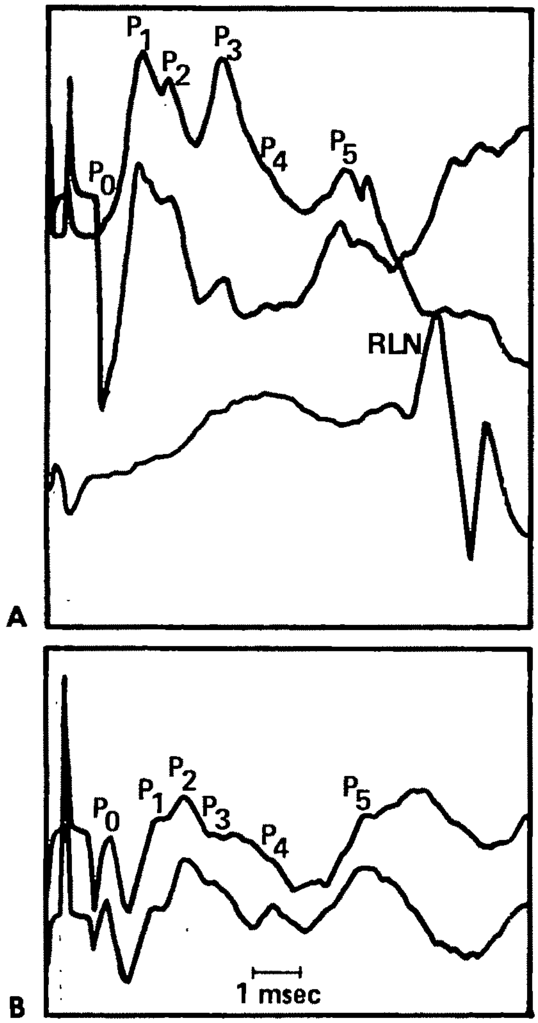

Fig 3. Laryngeal brain stem evoked response (LBR). A) Upper tracings are recordings of LBR from one paralyzed cat with C-3 and pharyngeal electrodes. Lower tracing is recurrent laryngeal nerve (RLN) response (see text). B) Example of two LBR recordings in same unparalyzed cat with Cz and C-3 electrodes.

cording was done both prior to and following paralysis in three animals. Mechanical ventilation was instituted with use of an FiO_2 of 21% (room air). Arterial blood gases were drawn at the start and conclusion of recording sessions to confirm that arterial pH, PO_2, and PCO_2 had been maintained within physiologic limits. Additional pancuronium bromide (0.1 mg/kg) was given to ensure adequate relaxation; ketamine HCl and xylazine anesthesia was continued throughout each experiment as noted above.

The SLN was stimulated with a Nicolet constant current stimulator (NIC 1003A) using 0.1-ms square waves administered as a stimulus train of 100 to 400 stimuli. Stimulus artifact was minimized by alternating polarity of the electrical stimulus. Both LBR, as measured between pharyngeal and C-3 electrodes, and RLN or LAR were amplified (x10,000) with a Nicolet physiologic amplifier (model HGA-200A) and were recorded simultaneously by an averaging computer triggered by the SLN stimulus pulse (Nicolet CA-1000, band pass 300 to 1,500 Hz, sensitivity ±10 μV). The LBR and evoked RLN response were plotted with a Nicolet x-y plotter. No animal experienced significant cardiovascular effects from repetitive SLN stimulation. Unparalyzed animals experienced no apnea secondary to repetitive SLN stimulation.

Stimulus intensity was varied between 0.2 and 2 mA in 0.2-mA steps, stimulus frequency was varied between 1/s and 8/s, and number of samples was varied between 100 and 400 to assess the effect of these changes on the LBR. Each stimulus condition was repeated twice to demonstrate response replicability. Peak and interpeak latencies were measured. In six animals, the generator source of LBR waves was investigated by sectioning the vagus nerve at the base of the skull and the SLN just proximal to the stimulating electrodes.

RESULTS

Stimulation of the internal branch of the SLN evoked six positive and five negative waves with reproducible latencies measured between C-3 and pharyngeal electrodes. The waves are labelled P0 through P5 and N0 through N4. Figure 3A is a sample tracing showing both LBR (two tracings from the same cat) and RLN response. Waves P0 and N0 were inconsistently present, but reproducible when seen. With use of different surface electrode montages, an LBR was elicited with little muscle artifact in an unparalyzed animal. Six positive and five negative waves with similar latencies but different waveform morphology than with C-3–pharynx were seen (Fig 3B). The most useful montage appeared to be Cz and C-3, eliminating the pharyngeal electrode that would predictably cause most muscle artifact.

Multiple recordings were taken from each cat at intensities ranging from 0.2 to 2.0 mA. Response thresholds varied between 0.4 and 0.6 mA. Latency-intensity functions of waves P0 through P5 were constructed; although the latencies of P1 through P3 decreased slightly with increased intensity, the differences were not statistically significant (Fig 4A).

The number of samples was varied from 100 to 400, and stimulus frequency was varied from 1/s to 8/s. Waves P0 through P3 showed a slight increase in latency with an increase in sample number (Fig 4B). With an increase in stimulus frequency, waves P1 through P4 showed a slight increase in latency with increase in frequency (Fig 4C). Again, these changes did not meet criteria for statistical significance.

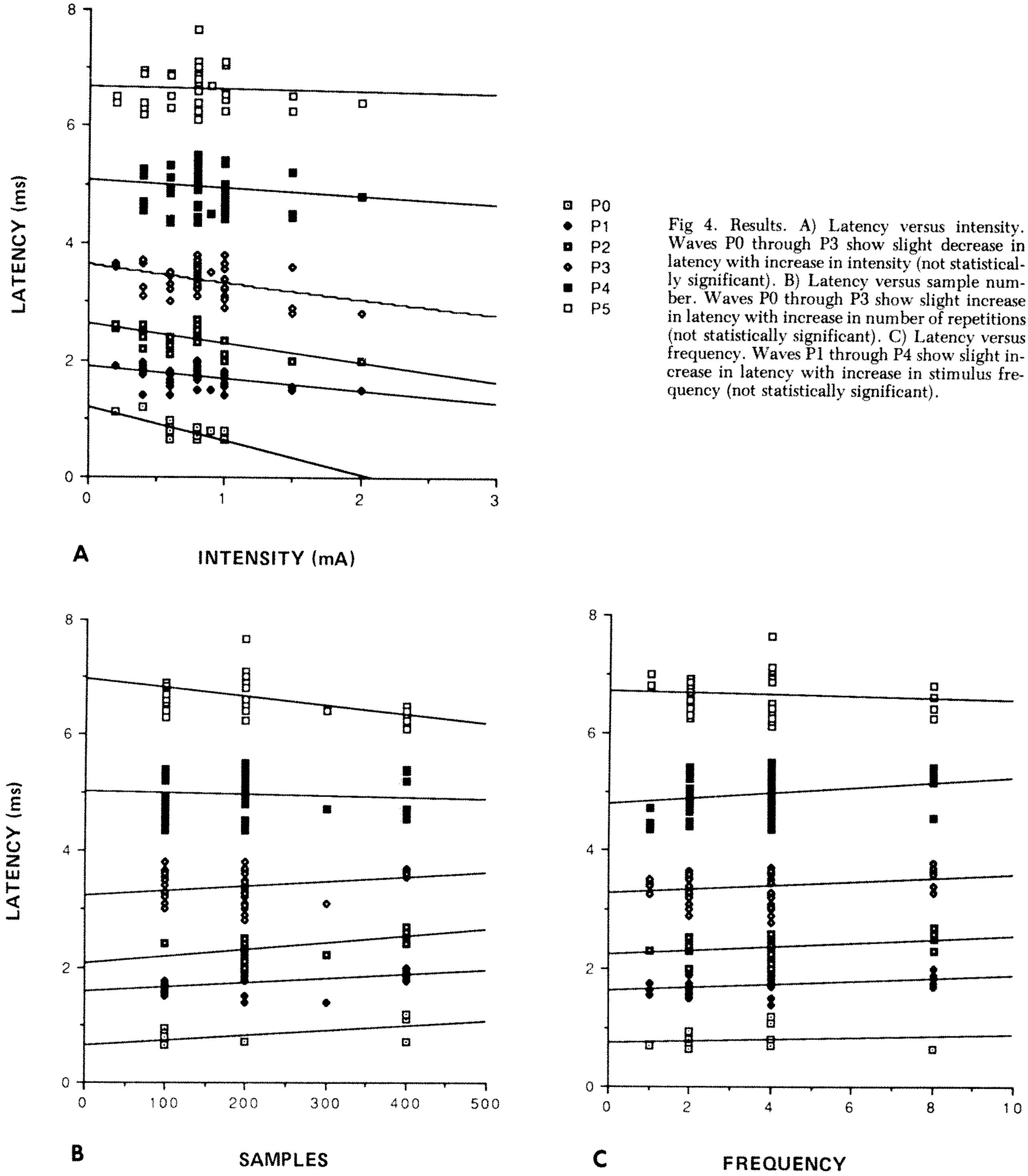

Fig 4. Results. A) Latency versus intensity. Waves P0 through P3 show slight decrease in latency with increase in intensity (not statistically significant). B) Latency versus sample number. Waves P0 through P3 show slight increase in latency with increase in number of repetitions (not statistically significant). C) Latency versus frequency. Waves P1 through P4 show slight increase in latency with increase in stimulus frequency (not statistically significant).

In summary, changes in parameters appeared to affect some waves slightly, but these effects were not found to be statistically significant. On the basis of evaluations of quality of tracing and threshold determination, the optimal recording parameters for this experimental model appeared to be 0.8 mA (suprathreshold), 400 repetitions, and a frequency of 4/s.

Because statistically significant latency changes did not appear under different stimulus conditions, all waveforms were pooled to calculate mean latency and standard deviation for each wave (Table 1). Waves P0 and N0 were not predictably present in all cats, and many cats had a P1-P2 complex reflecting the lower number of samples (N) for these waves. The mean latency of RLN response was 8.43 ms (range, 6.8 to 9 ms; SD = 0.40).

Transection of the vagus nerve just proximal to the nodose ganglion eliminated all waves except the P1 or P1-2 complex in some cats. Transection of the

TABLE 1. LARYNGEAL BRAIN STEM EVOKED RESPONSE MEAN LATENCIES

Wave	*Latencies (ms)*	*Standard Deviation*	*Range*	*N*
P0	0.78	0.15	0.65-1.20	21
P1	1.73	0.16	1.40-2.00	60
P2	2.37	0.19	2.00-2.70	34
P3	3.39	0.25	2.80-3.80	60
P4	4.96	0.35	4.35-5.50	54
P5	6.65	0.32	6.10-7.10	47
N0	1.10	0.15	0.70-1.30	20
N1	2.13	0.23	1.70-2.40	27
N2	2.76	0.26	2.15-3.15	60
N3	4.07	0.37	3.40-4.80	55
N4	5.52	0.29	5.05-6.20	55
Interpeak	4.93	0.31	4.30-5.30	46

SLN just proximal to the electrodes eliminated all LBR activity.

DISCUSSION

Validity of Response. In the present cat model, six positive and five negative waves were recorded from the brain stem with use of a far field technique with electrical stimulation of the SLN as a trigger. The fact that these waves occurred prior to the RLN response (Fig 3A) establishes that they exist in the appropriate time frame. Each recording was reproducible within the same animal; consistent responses to stimuli of alternating polarity further confirm their identity as nonrandom activity triggered by stimulation of the SLN. Transection of the SLN abolished all six waves, also establishing the response as an event-related potential.

Study Comparison. The experimental design of this project was similar to that used by Isogai et al,[13] who described four positive and four negative waves (P1 through P4 and N1 through N4) with reproducible latencies. Latencies of P0, P1, and N4 in the present study correspond to latencies of P1, P2, and N4 in the study of Isogai et al[13]; latencies for other waves, however, differ slightly (Table 2[14-18]).

There are a number of possible explanations for these differences. Reports in the literature as well as the present study confirm that procedural variation in placement of stimulating, recording, or ground electrodes can produce a marked difference in waveform morphology and polarity.[19] Latencies also can be altered by electrode position, either directly, or indirectly with changes in waveform morphology. Differences in filter settings, particularly the low frequency, can affect both waveform morphology and latency. Changes in P_{O_2} and P_{CO_2} can change latencies and amplitudes of evoked laryngeal brain stem recordings as reported by Isogai et al.[13] Additional factors that may affect latency of laryngeal evoked potentials are type and level of anesthesia, age, sex, and temperature. Characteristics of other sensory evoked potentials such as the ABR or the visual evoked response can be altered by factors such as type and level of anesthesia, hypothermia, and oxygenation; the LBR is probably no exception.[19] Procedural variation, including electrode placement and filter settings, is most plausible as an explanation for differences in these two studies. Amplitudes did not appear consistent within animals and will not be discussed further.

TABLE 2. LATENCY COMPARISON

Present Study	*Isogai et al*[13]	*Near Field Data*
P0: 0.78 ms N0: 1.10 ms P1: 1.17 ms	P1: 0.5-1.0 ms N1: 1.2-1.4 ms P2: 1.6-2.3 ms	Ipsilateral vagus nerve 1.1 ± 0.9 ms (Lucier and Sessle[16])
P2: 2.37 ms N2: 2.76 ms P3: 3.39 ms	P2: 1.6-2.3 ms N2: 2.4-2.7 ms P3: 2.8-3.2 ms	Nucleus solitarius 1.3-3.5 ms (Biscoe and Sampson,[14] Sessle,[15] Porter[17])
P4: 4.96 ms N4: 5.52 ms	P4: variable N4: 5.0-5.5 ms	Nucleus ambiguus 5-10 ms (Porter,[17] Delgado-Garcia et al[18])
P5: 6.65 ms		?? Reticular formation 7 ms (Sessle[15])

Parametric Studies. Repetition rate was varied between 1/s and 8/s without significant effect on latencies. Increase in repetition rate is known to degrade response in other sensory evoked potentials.[19] It is important to establish the most rapid rate that will not alter the waveform or latency significantly, because this will reduce the time needed for test completion. Rates up to 8/s did not appear to degrade the LBR in this study.

Latencies of ABR are known to decrease, and amplitudes increase, with an increase in stimulus intensity.[19] Latencies in this study did not change significantly with increase in intensity. While recruitment in the cochlear system may result in a more rapid and larger brain stem response, the laryngeal system could behave in an all-or-none fashion, as it is a protective reflex. The small size of the present study may be another possible explanation for the difference in latency response to varying intensities of the ABR and the LBR.

Generator Sources. There have been numerous studies of near field recordings in the brain stem after stimulation of the SLN. Anatomic and electrophysiologic studies following stimulation of the internal branch of the SLN have revealed the polysynaptic pathway to be as follows: vagal afferents through the nodose ganglion to the nucleus solitarius, which communicates with the nucleus ambiguus, stimulating laryngeal adductors via the RLN. Neurons in the reticular formation are stimulated also (Fig 1).[7,8,11,12,14-16,20,21] These studies have not only defined the afferent and efferent pathways, but also have calculated latencies of the response between two points in the pathway. Comparison of near field latencies with far field latencies allows speculation as to the generator source for each wave.

Isogai et al[13] postulated P1, N1, and P2 to be generated by the ipsilateral vagus nerve on the basis of an increase in recorded amplitude when a positive recording electrode was placed adjacent to the ipsilateral vagus nerve. Lucier and Sessle[16] measured the conduction time of orthodromic stimuli from the SLN to the nodose ganglion as 1.1±0.9 ms, corresponding nicely with the P1 and N1 latencies reported by Isogai et al[13] and the P0, N0, and P1 latencies in the present study (Table 2[14-18]). In both the study of Isogai et al and the present study, earlier waves failed to disappear after transection of the vagus nerve, suggesting the generator source of these waves to be the vagus nerve.

Near field evaluation of response latencies in the nucleus solitarius after stimulation of the ipsilateral SLN have ranged from 1.3 to 3.5 ms.[14,15,17] This nucleus is known to be the first one involved in this afferent pathway.[8,16,20] The measured latencies of the P2, N2, and P3 of Isogai et al[13] and the present study's P2, N2, and P3 correspond to near field data reported by Porter,[17] Biscoe and Sampson,[14] and Sessle[15] (Table 2[14-18]).

The latencies of N4 in both far field studies and P4 in this study correlate with near field data revealing orthodromic latencies of 5 to 10 ms from the SLN to the nucleus ambiguus.[16-18] In the present study, a repeatable P5 with a mean latency of 6.65 ms was found across animals. We postulate this component to be generated by interneurons or neurons located in the reticular formation. Although anatomic studies have not revealed fiber projections from the internal branch of the SLN to interneurons or the reticular formation, Sessle[8] has found mean response latency to SLN stimulation for reticular formation neurons of 7 ms.

In summary, the potential use of LBR as a research tool to study the polysynaptic reflex pathway is readily apparent. However, if adapted for use in humans, it may also have tremendous clinical application. Further electrophysiologic definition of this reflex pathway in humans is not feasible if an operative procedure and paralysis are required. In the present study, a different electrode montage (Cz and C-3) was used in both sedated and unparalyzed cats to eliminate muscle artifact. Latencies of LBR waves were reproducible and very similar to those found with C-3 and pharyngeal electrodes. Further studies using Cz and C-3 recording electrodes are ongoing. The final step toward human application will be institution of transcutaneous SLN stimulation to eliminate the need for an operative procedure.

In order to establish the location of anatomic structures that generate surface recorded evoked potentials, it will be necessary to compare results of far field brain stem recording with intracranial recordings or lesion studies, as has been done with other evoked potentials. The ABR and other sensory evoked potentials have had a great influence on diagnosis, prognosis, and monitoring of neurologic disorders. A better understanding of brain stem control of laryngeal function may be helpful in treatment of conditions such as idiopathic laryngospasm, spastic dysphonia, and sudden infant death syndrome, and may aid in the diagnosis and rehabilitation of laryngeal dysfunction in the brain injured patient.

ACKNOWLEDGMENT — The authors thank Hugh Lusted, PhD, for technical advice.

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SAN FRANCISCO OTOLOGY UPDATE: 1989

A course entitled San Francisco Otology Update: 1989, will be held November 2-4, 1989, at the Mark Hopkins Hotel in San Francisco. For further information, contact Extended Programs in Medical Education, University of California, Room U-569, San Francisco, CA 94143-0742; (415) 476-4151.

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PAN AMERICAN ASSOCIATION OF OTORHINOLARYNGOLOGY-HEAD AND NECK SURGERY

The XXII Congress of the Pan American Association of Otorhinolaryngology–Head and Neck Surgery will be held November 23-27, 1990, in Catagena, Colombia. For further information, contact Pedro Blanco, President, Pan American Congress, Hospital Universitario del Valle, 3er Piso Servicio de Otorrinolaringologia, Cali, Colombia.

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COMPLICATIONS FOLLOWING RHINOTOMY

REVIEW OF 148 PATIENTS

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For the period 1974 to 1988, 148 patients undergoing 162 rhinotomies at The Mount Sinai Medical Center, New York, for a variety of benign and malignant neoplasms were reviewed with particular attention to postoperative complications. The effects of certain predisposing factors such as prior rhinotomy, lateral versus total rhinotomy, additional medial maxillectomy or craniofacial resection, and preoperative irradiation or nasal bone erosion are discussed. In addition, a surgical technique of rhinotomy with medial maxillectomy is presented that includes maneuvers designed to prevent these complications.

KEY WORDS — paranasal sinus neoplasms, postoperative complications, rhinotomy.

INTRODUCTION

Lateral rhinotomy is a term used to describe those procedures that allow exposure of the nasal cavity through its lateral wall. In its strictest sense, the lateral rhinotomy is merely an incision along the side of the nose.[1] Using this incision with division of the nasal ala provides only limited access to the anterior nasal septum, pyriform aperture, and anterior surface of the inferior turbinates. In the classic lateral rhinotomy, a unilateral nasal osteotomy is performed and both the nasal ala and lateral aspect of the nose are reflected medially, allowing additional but still limited exposure of the nasal cavity. In the total rhinotomy, the columella, septum, and root of the nose are transected and the entire nasal pyramid is reflected to one side. Even with this more extensive technique, access is gained only to the anterior aspect of the nasal cavity.

A rhinotomy may be performed to remove those lesions limited to the nasal cavity and adjacent paranasal sinuses, or to aid in gaining additional exposure for the resection of larger lesions that involve the nasopharynx, parapharyngeal space, infratemporal fossa, or anterior cranial vault. In the latter instance, the rhinotomy incision can be extended infraorbitally and through the lip as in the Weber-Ferguson incision, or it can be combined with transpalatal, transcervical, mandibular splitting, or craniofacial approaches.

To remove those lesions that arise from the lateral nasal wall and extend into the contiguous sinuses, the rhinotomy can be combined with a medial maxillectomy. This permits en bloc resection of the lateral nasal wall and medial aspect of the orbit and maxilla.

It is the purpose of this paper to review our experience with the rhinotomy procedure and to analyze the postoperative complications of the various modifications of the operation and describe a technique designed to prevent them.

HISTORICAL REVIEW

Although lateral rhinotomy was first described by Michaux in 1848 and Brüns in 1872, the technique was not formally presented until 1902 by Moure.[1,2] The total rhinotomy first was described in the United States by Bordley and Longmire[3] in 1949. Their technique involved making a curvilinear incision across the bridge and along the side of the nose, osteotomies across both the nasomaxillary and nasofrontal sutures, transection of the columella and septum, and a submucous resection of the remaining intranasal portion of the septum. A secondary brow incision for exposure of the ethmoid and frontal sinuses also was described. In 1957 and 1960, Bordley and Linthicum[4] and Bordley and Cherry[5] reported on 40 patients undergoing rhinotomy for a variety of indications, including chronic polypoid sinusitis, localized osteomyelitis, and neoplasms of the nasal cavity.

In 1968, Doyle[6] described a modified lateral rhinotomy in which exposure of the anterior face of the maxilla and medial orbital wall enabled en bloc resection of the lateral nasal wall and ethmoid labyrinth. The technique reported was essentially a medial maxillectomy. It involved making a lateral rhinotomy incision that began at the level of the medial canthus. There was no brow extension, and the columella and septum were left intact. A low nasal osteotomy through the nasomaxillary process was performed in conjunction with the bony cuts of a medial maxillectomy. Doyle's series of cases consisted of two patients with an angiofibroma, two

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with an inverting papilloma, and one with an esthesioneuroblastoma, all of whom were treated successfully with this procedure.

Numerous reports during the 1970s emphasized the versatility of the rhinotomy approach for the surgical management of lesions arising from the nasal cavity, paranasal sinuses, and nasopharynx. In 1973, Neel et al[7] reported 56 cases of angiofibroma removed by a lateral rhinotomy approach in which the upper lip was split and a cheek flap created. In a recent update, Bremer et al[8] emphasized the superiority of the lateral rhinotomy approach for the removal of an additional 29 angiofibromas. Mabry and Fincher[9] reported on three patients who had resection of malignant melanoma involving the lateral nasal wall and ethmoid utilizing the modified lateral rhinotomy described by Doyle. In 1977, Djalilian et al[10] reported a series of 14 patients with esthesioneuroblastoma who underwent a total of 19 lateral rhinotomies for excision of their tumors. The technique involved removal of the nasal and lacrimal bones, lamina papyracea, and floor and anterior wall of the frontal sinus, together with the medial half of the orbital floor and anterior wall of the maxilla. The tumor and cribriform plate then could be removed.

Several authors reported the utilization of the lateral rhinotomy for the resection of inverting papillomas. As this tumor is usually a localized lesion of the lateral nasal wall that can extend into the ethmoid, antrum, or beyond, it is considered to be an ideal lesion for removal by a modified lateral rhinotomy or rhinotomy with medial maxillectomy approach. The superiority of this latter approach over intranasal procedures for the complete removal of the inverted papilloma has been confirmed by the publications of Suh et al,[11] Vrabec,[12] Calcaterra et al,[13] and Myers et al,[14] all of whom noted a decreased recurrence rate following rhinotomy.

Modifications of the rhinotomy operation have been proposed to reduce the incidence of both intraoperative and postoperative complications. Pope[15] added transantral ligation of the internal maxillary artery to the procedure to decrease intraoperative bleeding. Schramm and Myers[16] described marsupializing the transected lacrimal sac to the surrounding soft tissue to preclude postoperative stenosis and epiphora and reapproximating the medial canthal ligament to the periosteum of the nasal bone to avoid telecanthus. In addition, they utilized a plaster external splint and transnasal wires secured over buttons to prevent nasal collapse.

It was not until 1977 that Sessions and Larson[17] coined the term "medial maxillectomy" for the en bloc resection of the ethmoid labyrinth and medial maxilla along with portions of the lacrimal and palatine bones. Their procedure differed from the modified lateral rhinotomy described by Doyle,[6] in that the lip was split and a cheek flap created, and the osteotomies were modified to preserve the infraorbital rim, anterior crest of the maxilla, and nasolacrimal system. This medial maxillectomy technique was revised later by Sessions and Humphrey[18] to eliminate the lip-splitting incision, transect the lacrimal sac, and reapproximate the medial canthal ligament to the nasal bone. Transecting the lacrimal sac enhanced orbital retraction and reduced the postoperative edema of the lacrimal duct caused by intraoperative stretching. Lacrimal drainage was restored intraoperatively by the temporary placement of a polyethylene tube stent into the sac and securing it to the nasal septum.

In 1980, Bridger[19] extended the lateral rhinotomy with either an osteoplastic frontal craniotomy or transfrontal sinusotomy for removal of ethmoid lesions that extended intracranially. Barton[20] presented 32 cases of squamous cell carcinoma of the lateral nasal wall that were managed surgically by lateral rhinotomy with medial maxillectomy. In 1984, McGuirt and Thompson[21] reviewed the applicability of rhinotomy for resection of malignant tumors of the nasal septum. Lateral rhinotomy alone was adequate only for the removal of anterior septal tumors. Posterior tumors required an additional sublabial incision with retraction of the upper lip superiorly. Rhinotomy combined with a lip-splitting incision permitted resection of the septum and floor of the nose.

In a review by Mertz et al[1] of 226 extended lateral rhinotomies, the lesions resected were benign in 43% of the cases, malignant in 55%, and mixed in 2%. In conjunction with the basic lateral rhinotomy, 133 operations involved brow extensions, 80 involved lip-splitting procedures, 31 involved infraorbital incisions, and six involved temporal extensions. The procedures ranged from rhinotomy alone to total maxillectomy with orbital and infratemporal resections.

Most recently, the senior authors (H.F.B. and W.L.) introduced the superior rhinotomy.[22] In this procedure, the soft tissue and bony attachments of the nose were divided bilaterally and across the nasal root, hinging the nose downward on its remaining alar and columellar attachments. This was combined with bilateral medial maxillectomies and frontal craniotomy, permitting the en bloc resections of bilateral ethmoid neoplasms with intracranial extension.

MATERIALS AND METHODS

All available records were reviewed of those patients undergoing a rhinotomy by the senior authors as the central operative procedure for extirpation of a nasal or paranasal sinus lesion at The Mount Sinai Medical Center, New York, from 1974 through 1988.

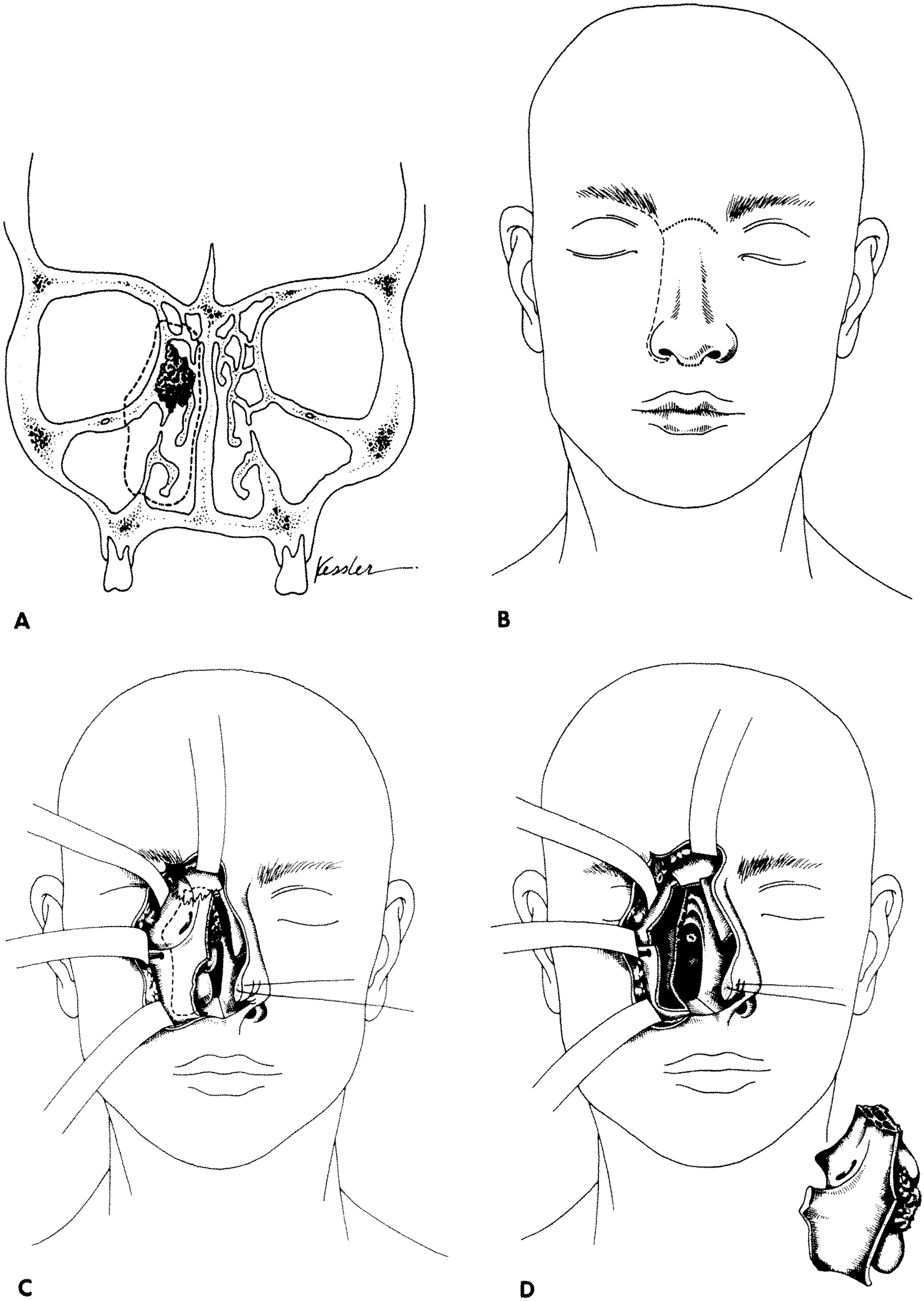

Fig 1. Lateral rhinotomy with medial maxillectomy. A) Coronal view of resection margins. B) Incision for lateral rhinotomy (dashed line) and total rhinotomy (dashed and dotted lines). C) Outline of osteotomies. D) Postoperative defect with specimen removed.

The records included those patients undergoing rhinotomy alone or in combination with medial maxillectomy, bifrontal craniotomy, mandibulotomy, or partial maxillectomy with splitting of the upper lip. The charts of those patients undergoing total maxillectomy alone or in combination with orbital or infratemporal exenteration were excluded, as this more radical procedure had an accompanying higher rate and severity of postoperative complications.

Each record was reviewed with regard to the type and size of the lesion, the extent of surgery performed, a history of prior surgery or preoperative radiation therapy, and the complications encountered. Complications were classified as immediate if they occurred within the 48-hour perioperative period, early if they were present within the first few weeks postoperatively, and late if they persisted or required surgical correction. Late complications were separated into those that were primarily functional and those that were cosmetic in nature.

TECHNIQUE

One hundred twenty of the 162 rhinotomies (74%) in this series were combined with a medial maxillectomy, making this the most common procedure performed. Although the rhinotomy with medial maxillectomy technique to be presented is similar in certain respects to those previously reported, additional maneuvers are described that both ensure adequate tumor removal and minimize postoperative complications. The technique is applicable for those lesions that necessitate en bloc resection of the ethmoid labyrinth with the medial maxilla (Fig 1A). With lesions located along the lower lateral nasal wall in the region of the inferior turbinate or meatus, the incision can begin at the level of the medial canthus, and a brow extension or ethmoidectomy need not be performed.

Lateral Rhinotomy With Medial Maxillectomy. After the induction of general endotracheal anesthesia, two tarsorrhapy sutures of 5-0 silk are placed. A curvilinear skin incision begins beneath the medial aspect of the eyebrow and runs downward in the nasofacial and alar sulci, ending within the nostril (Fig 1B). The incision is deepened in layers, with hemostasis accomplished by electrocautery of the angular vessels and their branches. The incision is carried down to the underlying bone, with the periosteum over the face of the maxilla and its frontal process raised with a free elevator. Continued elevation of the periosteum in the medial aspect of the orbit results in detachment of the medial canthal ligament from the anterior and posterior lacrimal crests. The lacrimal sac is displaced carefully from the fossa and retracted laterally. The periorbita is elevated further, and the globe is displaced laterally with either a small malleable ribbon or a rigid orbital retractor. The anterior ethmoid artery then is identified in the frontoethmoidal suture line, cauterized, and divided close to its foramen. The posterior ethmoid vessels are not divided, but remain as a landmark to identify the anterior wall of the sphenoid sinus and to avoid inadvertent injury to the optic nerve. The lacrimal duct is now put on stretch by further lateral retraction of the globe and lacrimal sac. The duct is divided as it enters the lacrimal bone, permitting exposure of the entire medial and inferior portions of the orbit.

The nasal ala is detached by dividing the vestibular lining with a scalpel or scissors. A lateral osteotomy of the nasal pyramid is performed low along the frontal process of the maxilla with a straight chisel or oscillating saw. The bone then is out-fractured and retracted to the opposite side along with the soft tissues of the nose, with a 2-0 silk suture passed through the ala. The periosteum of the anterior face of the maxilla is now elevated, with care taken not to injure the infraorbital neurovascular bundle. A small antrotomy then is made with a mallet and gouge through the canine fossa and enlarged with a Kerrison rongeur. If there is no evidence of extension of disease into the lateral recess, posterior wall, or floor of the antrum, the osteotomies of the medial maxillectomy can be performed.

The first bone cut is made with either an osteotome or a Kerrison rongeur from the antrotomy across the pyriform rim into the inferior meatus at the level of the floor of the nasal cavity. A second cut then is carried backward in the inferior meatus through the posterior wall of the antrum with either heavy right-angled scissors or a chisel. The third bone cut is made with a chisel or Kerrison rongeur upward from the antrotomy to the infraorbital rim medial to the infraorbital foramen. Within the orbit a fourth osteotomy is made along the frontoethmoidal suture line, by angling the chisel slightly downward to avoid entering the anterior cranial fossa or injuring the cribriform plate. The cut is carried back, but does not violate the posterior ethmoid vessels. This superior cut encompasses the ethmoid labyrinth, as well as the middle turbinate. Anteriorly, the remaining portion of the frontal process of the maxilla is sectioned above the lacrimal fossa to join the lateral nasal osteotomy. A fifth osteotomy then is made with a chisel downward and forward from the frontoethmoid suture line at the level of the posterior ethmoid artery toward the infraorbital rim cut (Fig 1C). Finally, a cut is made upward posteriorly, just in front of the pterygoid plates, with angled scissors. This divides the party wall between the antrum and the nasal cavity behind the posterior margin of the inferior and middle turbinates. The specimen now is engaged with a tenaculum and, by rocking it and dividing the remaining soft tissue attachments with scissors, it is

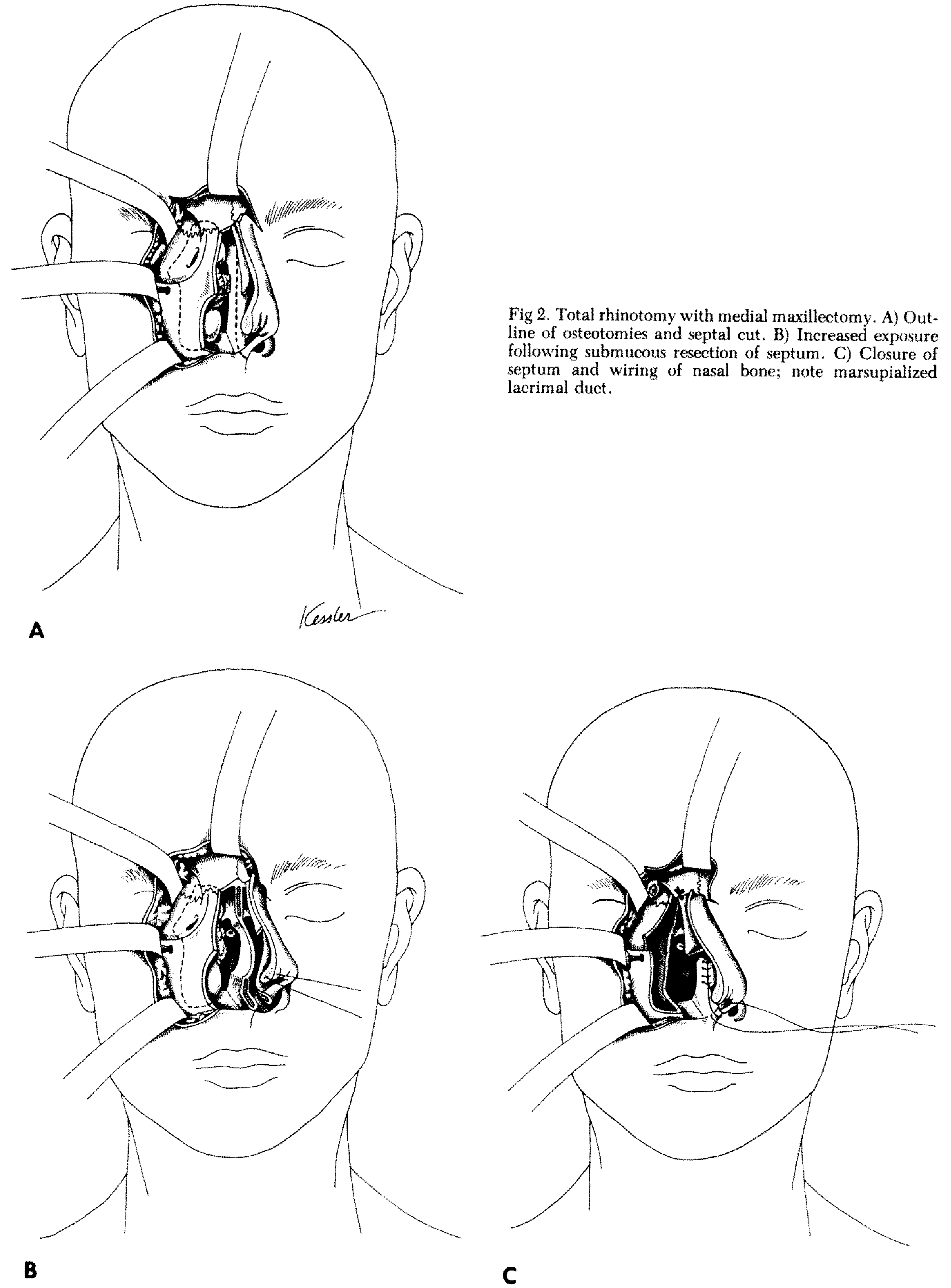

Fig 2. Total rhinotomy with medial maxillectomy. A) Outline of osteotomies and septal cut. B) Increased exposure following submucous resection of septum. C) Closure of septum and wiring of nasal bone; note marsupialized lacrimal duct.

removed (Fig 1D). Bleeding from the torn branches of the internal maxillary artery often occurs and generally can be controlled with electrocautery. If there is continuous oozing, a posterior pack can be placed.

Prior to closure, the previously cut edge of the lacrimal duct is identified, it is split, and the mucosa is everted and attached with 4-0 chromic sutures to the surrounding tissues. This marsupialization helps prevent synechia formation and stenosis of lacrimal outflow. A thin Silastic or polyethylene tube may be placed into the duct to stent the opening. This tube is held in place with a 3-0 chromic suture through the adjacent tissue. The nasal cavity then is packed with bacitracin-impregnated gauze, and the nose is replaced to its original position. Wound closure is performed by approximating the deep periosteal layer with multiple interrupted 4-0 chromic catgut sutures. The medial canthal ligament is reattached to the periosteum overlying the nasal bone. When closing the subcutaneous layer in the area of the ala, extra support can be achieved by passing the alar fixation suture farther and deeper into the cheek tissues than into the nasal tissue to which it approximates. Previously placed hatch marks make exact skin realignment possible. A light Xeroform gauze dressing then is placed over the suture line, followed by a tip dressing. In the nonirradiated patient, the sutures are removed on the fifth postoperative day. The nasal packing then is removed and the patient is discharged on the seventh postoperative day.

Total Rhinotomy. If increased intranasal exposure over that afforded by the lateral rhinotomy is needed, a total rhinotomy can be performed. A horizontal incision is made at right angles to the lateral rhinotomy incision across the nasion. All the overlying soft tissues are divided down to bone. A second incision is made across the base of the columella. In making the alar and columellar incisions, it is important that they are separated by vestibular skin in order to prevent postoperative vestibular stenosis. After performing the low nasal osteotomy on the side of the rhinotomy, a small chisel is used in a perforating fashion to create an osteotomy across the frontonasal suture line. By use of heavy scissors, the columella and membranous septum are cut. The septum then is detached from the anterior nasal spine, and the cartilaginous septum is transected in the plane of the rhinotomy incision (Fig 2A). Cartilage is preserved both caudally and dorsally to support the nose after it is returned to its normal position. A contralateral lateral osteotomy is unnecessary for mobilizing the nasal pyramid. The nose is swung to the opposite side, causing a greenstick fracture of the contralateral nasal bone. A submucous resection of the remaining cartilaginous and bony septum is performed, and the septal leaves are retracted to the side opposite the lesion to gain wider exposure of the nasal cavity and sphenoid sinus (Fig 2B). The previously described medial maxillectomy now can be performed.

After the specimen is removed, the septum is splinted with sutures of 3-0 chromic catgut that are placed before the pyramid is returned to its original position. Holes then are drilled in the mobilized nasal bone and the nasal process of the frontal bone opposite it, and a 25-gauge wire is placed to further stabilize the pyramid. A 2-0 chromic catgut suture is used to reattach the caudal septum to the periosteum of the anterior nasal spine (Fig 2C). Both nasal cavities then are packed, and wound closure is performed as previously outlined.

RESULTS

From 1974 through 1988, 148 patients underwent a total of 162 rhinotomies at The Mount Sinai Medical Center, New York. There were 103 male and 45 female patients, ranging in age from 8 to 85 years, with a mean age of 52 years.

A variety of benign and malignant lesions were resected by use of the rhinotomy approach. Fifty-eight percent (86 of 148 patients) had benign lesions, the vast majority of which were inverting papilloma (66 of 86 patients). The next most common benign lesions were the angiofibroma and the angiomatous polyp, each occurring in four patients. Schwannoma, benign mixed tumor, and aspergilloma were present in two patients each. Leiomyoma, ossifying fibroma, hemangioma, giant cell tumor, osteoma, and ameloblastoma occurred in one patient each.

Forty percent of the lesions were malignant (59 of 148 patients). Esthesioneuroblastoma was the most common malignancy, occurring in 12 patients, followed by squamous cell carcinoma, undifferentiated carcinoma, and adenocarcinoma arising in eight patients each. Melanoma was present in seven patients, and adenoid cystic carcinoma in six patients. Leiomyosarcoma, solitary plasmacytoma, and chordoma occurred in two patients each, with single cases of rhabdomyosarcoma, hemangiopericytoma, lymphoma, and mucoepidermoid carcinoma. Only three patients had synchronous benign and malignant lesions. All were found to have inverting papilloma with a concomitant squamous cell carcinoma.

Prior surgical procedures had been performed in 43% of the patients (64 of 148 patients). The great majority (45) of patients had undergone intranasal procedures that included submucous resection, polypectomy, sphenoethmoidectomy, and antrostomy. A Caldwell-Luc procedure had been performed in 18 patients, a prior rhinotomy in eight, external ethmoidectomy and transpalatal excisions in three patients each, craniotomy in two, and an osteoplastic flap in one.

A total of 162 rhinotomies were performed in 148 patients. Among these, 139 rhinotomies (86%) were combined with some other procedure. The most common additional procedure was the medial maxillectomy, which was performed in 120 patients. A bifrontal craniotomy was used in conjunction with a rhinotomy for the combined craniofacial resection of 12 lesions: seven esthesioneuroblastomas, one ossifying fibroma, one undifferentiated carcinoma, one recurrent squamous cell carcinoma, one adenoid cystic carcinoma, and one melanoma. A mandibulotomy was required in three patients with tumor involvement of the pterygopalatine and parapharyngeal spaces (two angiofibromas and one schwannoma). Partial maxillectomy with splitting of the upper lip was performed in one patient with a giant cell tumor and another with an ameloblastoma of the medial maxilla. A transpalatal approach was used concurrently in one patient with an angiofibroma, and a transsphenoidal approach in one patient with a chordoma.

Seventeen patients had more than one rhinotomy for removal of their tumor: seven had rhinotomies prior to their surgery at The Mount Sinai Hospital, and ten had repeat rhinotomies for recurrent disease following their initial operation at The Mount Sinai Hospital. One patient underwent four rhinotomies for recurrent ethmoid adenocarcinoma. Three patients had three rhinotomies each: one for recurrent squamous cell carcinoma, another for recurrent inverting papilloma, and the third for recurrent melanoma. The remaining 13 patients each had only one repeat rhinotomy for a recurrence.

Complications occurred in a total of 32 patients (21%). There were no immediate complications that included significant bleeding and no perioperative deaths. Early complications occurred in 16 patients (11%), with 13 having transient blepharitis and lid edema, four having epiphora and intermittent dacryocystitis, and two experiencing transient diplopia. Two patients had postoperative CSF leaks that spontaneously resolved.

Late complications occurred in 24 patients (16%). Four patients had persistent and bothersome crusting and pain. Dacryostenosis requiring dacryocystorhinostomy occurred in four patients. Osteomyelitis developed in two patients. In both cases, the patients had undergone a craniofacial resection with resultant infection of the frontal craniotomy bone flap. Nasocutaneous fistula occurred in two patients, one requiring surgical closure. A frontal sinus mucocele that required removal formed in two patients.

Late cosmetic complications occurred in 15 patients (10%). Nasal collapse secondary to a combination of pyramid shift, saddle deformity, columellar collapse, and alar retraction occurred in ten patients. Cosmetically unacceptable scars developed in six patients: four had scars from incisions that were placed too laterally on the cheek, one had webbing near the medial canthus, and one had depilation in the medial portion of the eyebrow. Vestibular stenosis on the side of the rhinotomy occurred in two patients.

COMPLICATIONS

In spite of technical improvements in the rhinotomy procedure and its modifications, postoperative complications do occur. In the series of Mertz et al[1] of 226 patients, which included extended procedures, an immediate complication rate of 2% and a delayed complication rate of 15% was reported. The immediate complications consisted of hemorrhage in two patients, meningitis in one patient, and cardiac arrest in two patients. Among the delayed complications, epiphora and ectropion developed in 14 patients, nasal collapse, synechia and perforations in eight, unacceptable scars in five, CSF leaks in three, and frontal duct obstruction, hematoma, frontal sinus mucocele, and facial neuralgia in one patient each. Among the 13 lateral rhinotomies with medial maxillectomy reviewed by Myers et al,[14] six patients had epiphora, three dacryocystitis requiring dacryocystorhinostomy, and one diplopia. Among the ten patients of Sessions and Larson[17] also undergoing rhinotomy and medial maxillectomy, there were two instances of epiphora. In the collective review of 85 cases of rhinotomy with lip division performed for the removal of juvenile nasopharyngeal angiofibromas, Neel et al[7] and Bremer et al[8] described crusting and sequestrum formation in 18 patients, hemorrhage requiring transfusion in nine, dacryostenosis in four, diplopia and deafness in three, unsightly scarring in two, and septal perforation, oroantral fistula, and CSF leak in 13. One patient each had exotropia, proptosis, frontal headache, facial asymmetry, and cheek numbness.

In our series, a total of 32 patients (21%) developed complications: in 16 patients (11%) they occurred early and in 24 patients (16%) the onset was late. There were no immediate complications in our series.

Postoperative nasal crusting is inevitable and should be anticipated in practically every patient undergoing a rhinotomy, especially when combined with a medial maxillectomy. This generally subsides within 6 months as re-epithelialization of the denuded areas occurs. Good nasal hygiene with frequent crust removal, cautery of granulation tissue, and careful irrigation of the surgical cavity aids in both patient comfort and postoperative healing. Persistent crusting is more apt to occur in the irradiated patient. All four patients in our series who had persistent crusting and pain had prior radiation therapy.

Epiphora and associated dacryocystitis is a relatively common reported complication and results from inadequate drainage of the lacrimal system due to either edema or stenosis of the duct. In their original description of the medial maxillectomy, Sessions and Larson[17] maintained the integrity of the nasolacrimal drainage system and despite this noted a high incidence of epiphora that they believed to be secondary to ductal edema from intraoperative stretching. A decreased incidence of epiphora was observed when Sessions and Humphrey[18] later modified the technique by transecting the lacrimal sac and stenting it with a polyethylene tube. We have found that simple marsupialization of the cut end of the lacrimal duct to the surrounding nasal tissues provides adequate lacrimal drainage in most cases. However, the four patients in this series who developed postoperative epiphora and dacryocystitis eventually stenosed their lacrimal ducts and required a formal dacryocystorhinostomy at a later date. All four patients had undergone a medial maxillectomy, with one of them having either a prior rhinotomy or radiation therapy.

Transient postoperative diplopia is generally due to detachment of the trochlea that results from dissection along the superior aspect of the orbit. Reattachment of the orbital periosteum is usually sufficient to provide adequate support and function of the superior oblique muscle. Only two patients in our series had transient diplopia; one patient had undergone a craniofacial resection for esthesioneuroblastoma, and the other a medial maxillectomy for an inverting papilloma. Telecanthus is a reported complication following rhinotomy with medial maxillectomy. To prevent this, Sessions and Humphrey[18] advocated wiring of the medial canthal ligament to the remaining frontal process of the maxilla. We have not found telecanthus to be a postoperative problem if careful reapproximation of the deep periosteal layer is performed.

Other early complications reported in our series are blepharitis, lid edema, and CSF leak. Thirteen patients experienced significant transient lid edema and blepharitis postoperatively. This resulted from local tissue trauma during intraoperative retraction and interruption of the lymphatic drainage of the eyelids. Of the two patients who developed postoperative CSF leaks, one had undergone a combined craniofacial resection for an ossifying fibroma, and the other a lateral rhinotomy with medial maxillectomy for a previously irradiated ethmoid adenocarcinoma. In both cases, the dura was violated surgically, but the leaks resolved spontaneously.

Postoperative wound infection is not a reported complication following rhinotomy and was not observed in our series. Two patients who had undergone combined craniofacial resections subsequently developed an osteomyelitis of the bone flap that required removal.

Two patients developed a frontal sinus mucocele following rhinotomy with medial maxillectomy from interruption and stenosis of the nasofrontal duct. One patient had an undifferentiated carcinoma, and the other a recurrent inverted papilloma. This complication of frontal sinus mucocele following rhinotomy with medial maxillectomy has been reported twice in the literature.[1,23]

While nasocutaneous fistulas can develop postoperatively, they are more apt to occur in irradiated patients undergoing a rhinotomy combined with an ethmoidectomy alone or as part of a medial maxillectomy. In our series, the two patients who developed ethmoid-cutaneous fistulas had medial maxillectomies and perioperative radiation therapy. In the one patient, who had preoperative radiation therapy for a solitary plasmacytoma, the fistula eventually required closure with a nasolabial flap. In the second patient, who had postoperative irradiation for an adenoid cystic carcinoma, the fistula closed spontaneously. Neither patient had undergone a prior rhinotomy.

Most authors comment on the excellent cosmetic results following rhinotomy. However, a total of 15 patients (10%) developed late cosmetic complications in our series. Ten of these patients suffered nasal collapse attributable to shift of the nasal pyramid, saddle deformity, columellar collapse, or alar retraction. Of these ten patients, eight had undergone concurrent medial maxillectomy, six had total rhinotomies, six had perioperative irradiation, four had a prior rhinotomy, and only two had evidence of preoperative nasal bone erosion by tumor. Nine of the ten patients had significant septal perforation subsequent to surgical resection of the septum.

The nasal pyramid normally is supported laterally by the frontal process of the maxilla, centrally by the cartilaginous and bony nasal septum, at its root by the nasal process of the frontal bone, and caudally by the anterior nasal spine. In performing a rhinotomy with a medial maxillectomy, several maneuvers are performed in order to maintain this nasal support postoperatively. The lateral nasal osteotomy performed on the side of the medial maxillectomy is made low along the face of the maxilla in order to preserve as much nasal bone as possible. When transecting the columella and septum in a total rhinotomy, the caudal septum is disarticulated off the anterior nasal spine prior to making the septal cut. Good caudal and dorsal cartilaginous struts therefore are left attached to the nasal pyramid in order to prevent postoperative saddling. In closing the total rhinotomy site, the reflected nasal bone is rewired to the nasal process of the frontal bone, the transected septum is resutured, and the caudal septum is reapproximated to the periosteum of the anterior nasal spine. In addition to carefully closing the deep periosteal layer, extra alar support can be achieved with the previously described alar fixation suture. Despite these measures, nasal collapse occurred in ten patients. The most significant predisposing factor was the addition of a medial maxillectomy (eight patients). With removal of the medial maxilla, lateral nasal support is reduced, with the nose now being supported mainly by its attachment to the frontal bone, anterior nasal spine, and septum. Once this support is disrupted, as in the total rhinotomy (six patients), the nose tends to collapse toward the side of the medial maxillectomy cavity, especially in those patients who have lost septal support because of large perforations. With repeat rhinotomy (four patients), progressive nasal tilt and alar retraction can become more pronounced, especially with loss of the medial maxilla and septal support. Although perioperative irradiation (six patients) may adversely affect the healing process and exaggerate the nasal deformity following rhinotomy, it does not by itself cause nasal collapse. Nasal bone erosion (two patients) is another contributing cause to saddle deformity.

Vestibular stenosis occurred postoperatively in two patients who underwent total rhinotomy. This complication can be avoided by leaving an island of vestibular skin between the alar and columellar incisions that traverse the vestibule. Careful reapproximation of these separate vestibular incisions along with nasal packing will decrease the probability of stenosis.

The correct placement of the rhinotomy incision is important in achieving acceptable cosmesis. Many authors state that the incision always should be placed halfway between the nasal dorsum and medial canthus and then run inferiorly along the lateral aspect of the nose, medial to the nasofacial sulcus. Others state that the incision always should be placed more laterally, directly in the nasofacial sulcus. Clearly there is no standard formula that can be applied to all patients, and placement of the incision must be individualized. In patients with either very low or prominent nasal bridges, the incision should be placed closer to the nasofacial sulcus in order to avoid obvious scarring along the dorsum or lateral aspect of the nose. In patients whose noses are distorted preoperatively by expansile nasal tumor, correct incision placement may be difficult to assess, and wide scars that swing laterally onto the cheek may result (four patients). Care must be taken not to make the incision too close to the medial canthus, to avoid webbing (one patient). Also, incisions carried into the eyebrow must be bevelled in the direction of the hair follicles in order to avoid depilation (one patient).

CONCLUSIONS

The versatility of the rhinotomy procedure for removal of benign and malignant lesions of the nasal cavity and paranasal sinuses is well documented in the literature and the present series of 148 cases. The limited exposure afforded by a rhinotomy alone generally warrants an additional procedure, such as medial maxillectomy, external ethmoidectomy, total rhinotomy, or superior rhinotomy, depending on the type and extent of the lesion.

A surgical technique of rhinotomy with medial maxillectomy designed to provide adequate tumor removal and prevent postoperative complications has been presented. Nevertheless, a significant number of functional and cosmetic complications can be anticipated in those patients undergoing a total rhinotomy, medial maxillectomy, or repeat rhinotomy or having perioperative irradiation or nasal bone erosion.

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INDIRECT VIDEOLARYNGOSCOPY VERSUS DIRECT ENDOSCOPY FOR LARYNX AND PHARYNX CANCER STAGING

TOWARD ELIMINATION OF PRELIMINARY DIRECT LARYNGOSCOPY

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Thirty-nine patients with cancer of the larynx and pharynx (33 untreated and six previously treated patients) underwent tumor mapping by both direct laryngoscopy (DL) and indirect videolaryngoscopy (IVL). The examiner in each case was unaware of the findings of the other evaluation method. After definitive treatment had been carried out so that pathologic and operative information was also available, comparisons of the accuracies of the two methods of staging were made. In 32 cases, IVL provided information equal to or better than that provided by DL, and a tissue sample also could be obtained during IVL. On the basis of these findings, we conclude that aggressive, office-based IVL can guide initial treatment planning (partial or total laryngectomy versus irradiation) and patient counseling. A confirmatory DL can be performed without surprises at the time of definitive surgery, rather than as a separate procedure — a cost-effective modification of standard practice.

KEY WORDS — cancer, endoscopy, laryngoscopy, larynx, pharynx, staging, video.

INTRODUCTION

Traditionally, patients with suspected cancer of the larynx or pharynx undergo direct laryngoscopy (DL) with biopsy under general anesthesia, so that the surgeon can obtain a tissue diagnosis and "stage" or "map" the exact anatomic extent of the tumor. Only with this information can the surgeon counsel the patient and family specifically about the treatment options and, when appropriate, the most likely surgical procedure indicated. When surgery is the initial treatment chosen, the patient usually enters the hospital a second time for the definitive operation. Especially in the case of a proposed conservation procedure on the larynx, the patient grants permission for a bigger procedure, in case the tumor proves to be larger than was anticipated from DL and whatever radiographic studies were performed.

The authors have encountered situations in which adherence to the above approach was not possible because DL was not an option or was unsuccessful. Examples have included patients who were extremely frail medically, those with fixed temporomandibular joints limiting mandible excursion, one patient whose possible recurrence post-hemilaryngectomy was visible indirectly but could not be exposed endoscopically, another who refused DL because of a severe hospital phobia, and one from whom inadequate tissue for diagnosis was obtained at DL. In each of the above cases, the required information and tissue were obtained indirectly by one of the authors (R.W.B.) in a videoendoscopy laboratory, thus allowing treatment planning to proceed.

Having experienced success with indirect videolaryngoscopy (IVL) for tumor staging and biopsy in the circumstances just mentioned, we designed a study to answer the following questions: 1) To what extent can staging of head and neck tumors by IVL approximate the accuracy of that performed by DL? 2) How successfully can tissue be obtained by indirect biopsy? and 3) Are there tumors for which one method of staging is routinely superior to the other?

MATERIALS AND METHODS

Patient Group. Thirty-nine patients with suspected new or recurrent head and neck carcinomas were enrolled in this study from the combined caseloads of the authors at Loyola University of Chicago (Hines Veterans Administration and Loyola–Foster G. McGaw Hospitals) during the 14-month period between Dec 31, 1987, and March 1, 1989. The patient group is not a consecutive series, because logistical factors (patient transportation problems, temporary unavailability of the physician performing IVL staging, etc) prevented inclusion of some patients, but there were no preselection criteria used. Thirty-three patients were previously untreated. Of the six previously treated patients, five had received irradiation alone, and one had received surgery and irradiation.

General Procedure. Each patient underwent both staging procedures: IVL with or without biopsy in the Loyola University Voice Laboratory by one of the authors (R.W.B.) and traditional DL and biopsy by the other senior author (S.L.C.) or a chief resident (fourth year otolaryngology). With regard

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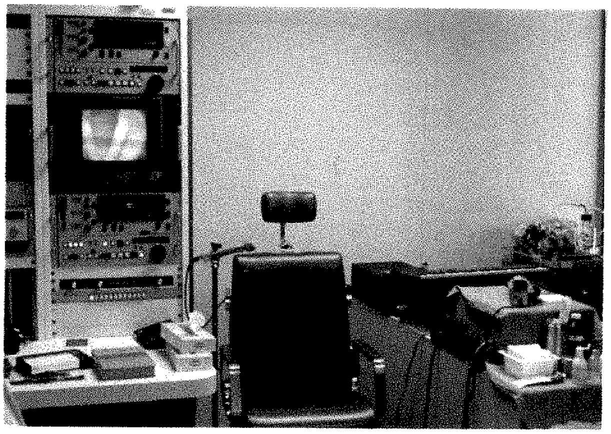

Fig 1. Voice and Videoendoscopy Laboratory, Loyola University of Chicago.

to training and qualifications of those doing the staging, both senior authors (R.W.B., S.L.C.) received equivalent training in head and neck cancer surgery at Washington University, St Louis (Dr Joseph Ogura). During the past 4 years at our institution, chief residents were trained in the same methods.

Standard staging diagrams of tumor extent were filled out at the conclusion of both IVL and DL, but were kept separate from the patients' records, with results unknown to the other endoscopist until both methods of tumor mapping had been completed. Besides drawing tumor boundaries, the endoscopists made notes on these diagrams about bulk, submucosal versus mucosal extent, pertinent mobilities (vocal fold, movement of pharyngeal tumors over prevertebral fascia), and so forth.

The order of DL versus IVL was not controlled. Twenty-nine patients were staged by IVL first, and ten, by DL. Reasons for staging by DL first included necessity for emergency tracheotomy, logistical problems with patient transport to the endoscopy laboratory prior to DL, and temporary unavailability of the physician performing IVL.

Techniques of Endoscopy. For IVL,[1] patients were examined while sitting in an examining chair (Fig 1). They received topical anesthesia as needed to palate, posterior pharyngeal wall, base of tongue, hypopharynx, larynx, and trachea (Xylocaine 10%, 4%, or 2% and/or cocaine 5%). Application techniques included direct spray, cannula instillation of the endolarynx, and cricothyroid membrane puncture with a short 25-gauge needle and syringe for subglottic introduction.

The Olympus ENF-P2 fiberscope and Wolf rigid 90° laryngeal telescope were available for coupling to a JVC Newvicon camera, Bruel & Kjaer strobe generator, and Sony BVU 870 U-Matic video recorder. One or both endoscopes were used as dictated by patient tolerance and the lesion involved. For example, the fiberscope was more useful for assessing subglottic and ventricular extent, while the rigid scope was better for panoramic views, particularly during manipulation of the epiglottis or aryepiglottic folds. Biopsy forceps were used to manipulate these structures when indicated to more fully assess tumor boundaries (Fig 2).

A variety of curved laryngeal forceps were used for transoral biopsy. In addition, a fiberoptic scope with biopsy channel became available during the study, but was not used for any biopsy attempt. Patient selection for biopsy was regulated only by management considerations, and not by patient factors or tumor site. No patients were sedated for biopsy. Nine of ten biopsies attempted were successful in providing an adequate tissue diagnosis.

A fully stocked "crash cart" was available for all procedures (in case of bleeding or allergic reaction to topical anesthesia), but was never needed.

Direct laryngoscopy was performed with general anesthesia and one or more of the following scopes:

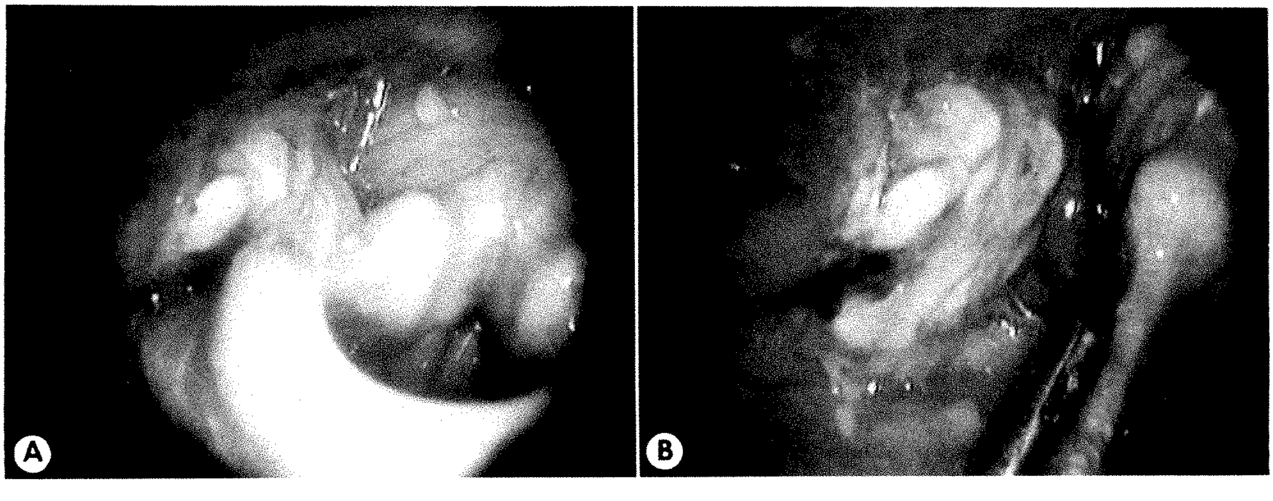

Fig 2. Videophotographs of tumor of right lateral pharyngeal wall and pyriform sinus. A) Viewed through rigid laryngeal telescope. B) With epiglottis displaced by biopsy forceps.

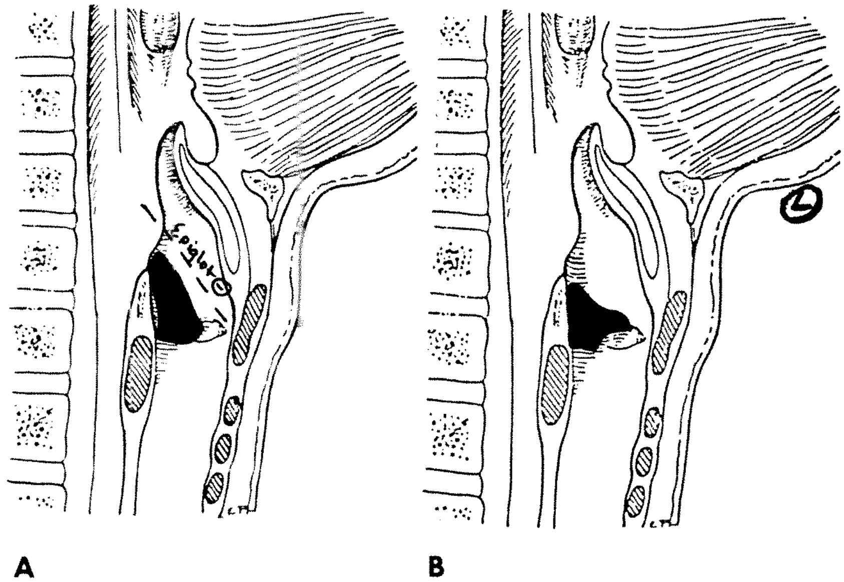

Fig 3. Staging diagrams of same laryngeal tumor, judged to be same stage. A) From direct laryngoscopy. B) From indirect videolaryngoscopy. L — left.

Holinger anterior commissure, Dedo, Jesberg, and, rarely, Bouchayer. A few patients undergoing surgery underwent DL only once, as the first step of the definitive operative procedure. More typically, DL was performed twice: once for preliminary staging and biopsy, and a second time as the first step of definitive surgery, to confirm tumor location and size. Surgical specimens were examined for details of tumor involvement and were compared with the staging diagrams. Specimens frequently were dissected by the surgeon, and specific areas were labelled and submitted separately for histologic examination.

Data Analysis. Tumors were categorized by sites according to the epicenter of involvement. For all patients, the authors compared IVL and DL diagrams. For patients whose DL and IVL staging diagrams were judged to differ, all available data including pathology reports, information gained intraoperatively, and the original indirect staging videotapes were reviewed by the authors in order to determine which staging diagram was more accurate (Figs 3 and 4).

RESULTS

HOW DID STAGING DIAGRAMS COMPARE?

Diagram pairs were classified as follows: equivalent in 21 patients, IVL more accurate than DL in 11, and IVL less accurate than DL in seven (Fig 5A). Of the 39 patients, 21 DL diagrams were provided by a chief resident, and 18 by an attending physician (Fig 5B).

WHAT WERE RATES OF DIAGNOSTIC SUCCESS FOR IVL AND DL BIOPSIES?

Indirect videolaryngoscopy biopsy returned a positive diagnosis in nine of the ten patients in whom it was attempted. A patient with an anterior commissure lesion could not undergo biopsy because of a combination of poor cooperation and technical difficulty. Biopsy at DL returned a defini-

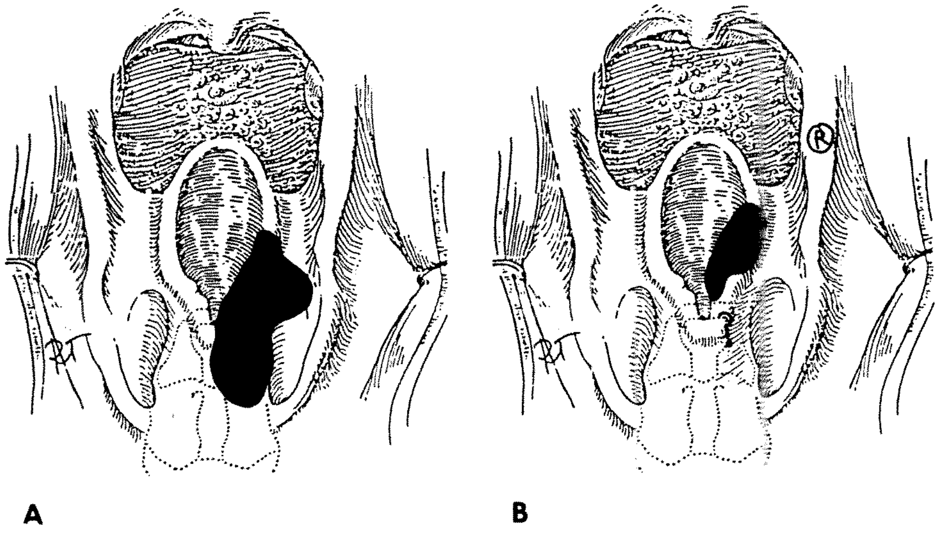

Fig 4. Staging diagrams of same tumor, judged to be different stages. A) From direct laryngoscopy. B) From indirect videolaryngoscopy. R — right.

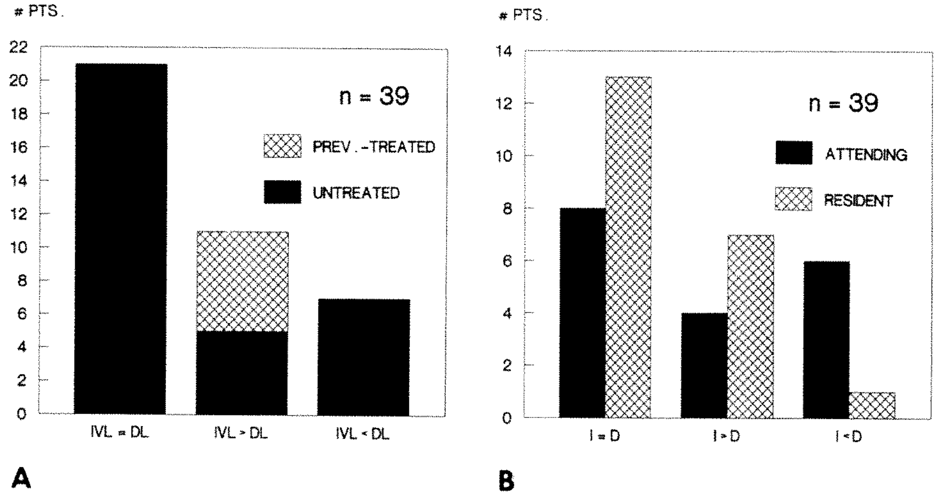

Fig 5. Indirect videolaryngoscopy (IVL) versus direct laryngoscopy (DL). A) Comparison of overall accuracies. B) Whether DL staging was done by attending physician or resident.

tive pathologic diagnosis in 28 of 29 attempts. In one instance, tissue obtained from what appeared to be an obvious tumor at DL returned a diagnosis of hyperkeratosis with atypia (proven to be cancer by IVL biopsy). In each case of failure, the other method of biopsy succeeded.

ARE SPECIFIC SITES MORE ACCURATELY ASSESSED WITH PARTICULAR METHOD OF STAGING?

Supraglottis (n = 14). In ten of these cases, IVL diagrams were judged to be equally accurate to those drawn during DL (Fig 6). In no instance was DL judged to be more accurate than IVL, and IVL was judged to be more accurate than DL in four patients. Three of these four patients had been treated previously. In one case, a small burrowing lesion at the anterior false vocal folds that was detected by IVL was not seen during DL until attention was directed to this area by the IVL staging diagram. In another DL diagram, the lesion was drawn too small and too far posteriorly on the false vocal folds and aryepiglottic folds. In a third case, epiglottic extent was understaged to be unilateral on DL, and the tumor also was drawn too far down on the false vocal fold. The fourth patient previously had undergone a supraglottic laryngectomy and postoperative irradiation, but developed a second primary tumor on the contralateral arytenoid mucosa. In contrast to IVL, DL of this patient failed to detect a small amount of lateral pharyngeal wall and tongue base involvement.

Glottis (n = 14). Of the seven pairs of IVL/DL staging diagrams judged to be different, IVL was judged to be more accurate than DL for five patients and less accurate than DL for two. In both cases of IVL failure, subglottic extent was recognized but understaged. The main deficit of DL diagrams judged to be less accurate than the corresponding IVL diagram was insufficient recognition of bilateral involvement, especially with superficial disease.

Margin (n = 5). Staging diagrams for two of five cases differed. In one, IVL suggested transglottic spread of the tumor, while DL more accurately predicted that the vocal fold was uninvolved. In the other case, DL placed the tumor too low on the arytenoid and false fold, while IVL more accurately showed these structures to be free of tumor.

Pharynx (n = 4). In three of these cases, DL was more precise in delineating tumor boundaries. However, in no case was there a gross inaccuracy of IVL.

Pyriform Sinus (n = 1). The DL diagram placed this lesion on the anterior wall of the pyriform sinus, while IVL more correctly located it on the medial wall.

Vallecula/Base of Tongue (n = 1). Both diagrams placed the lesion similarly; however, DL more correctly depicted a small amount of base of tongue involvement.

WHAT IS DIFFERENCE IN COST BETWEEN TWO METHODS OF STAGING?

Inpatient DL was more expensive than outpatient DL, which in turn was approximately six times as expensive as IVL.

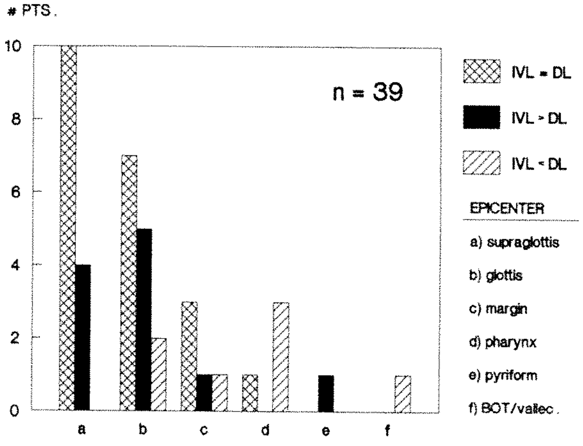

Fig 6. Comparison of accuracies of indirect videolaryngoscopy versus direct laryngoscopy, by site. BOT - base of tongue.

DISCUSSION AND CONCLUSIONS

In the initial design of this study, we considered comparing IVL with mirror/fiberoptic nasolaryngoscope examination as well as DL. However, on the basis of our combined previous experience, it was felt that undocumented mirror/fiberoptic examination was inadequate for treatment planning. Compared to mirror/fiberscopic examination alone, IVL entails a far higher degree of aggressiveness, with manipulation of structures as required for complete visualization, and it also results in a videotape that can be reviewed to focus on the boundaries of a given tumor.

The accuracy of IVL was, not surprisingly, the best for supraglottic tumors. Of 14 tumors in this site, none was staged incorrectly by IVL. Accuracy was also quite high for glottic tumors, with IVL shown to be the less accurate method in only two of 14 patients. If these sites are combined, IVL was judged to be superior to DL in nine of 28 cases, while DL was judged to be superior to IVL in only two of 28.

It is also interesting to note that IVL was judged to be more accurate than DL for all six previously irradiated patients. One possible reason may be that with the patient in the awake state a better appreciation of mobility, fullness, tissue "flexibility," and submucosal extent is possible.

On reviewing IVL videotapes of patients in whom DL was judged to be better than IVL, it was agreed mutually by the authors that in three of these seven patients, more faithful drawing on the diagram of what was clearly visible on the tape would have resulted in an IVL staging diagram equivalent to that obtained from DL. This observation reflects the important point that one is able to confirm and/or refine one's IVL staging at subsequent reviews of the videotape, while DL results in a staging diagram for which the data cannot be reviewed and refined after the patient leaves the operating room.

Another advantage of IVL is that patients and families are able to view the tumor for themselves, thus bringing a greater sense of reality to discussions of diagnosis and proposed treatment. It was observed informally that at least for some patients, this experience aided in motivating the patient and enhancing compliance. The risk of anesthesia during preliminary DL is eliminated also. The average total cost of outpatient DL and biopsy in our institution is approximately six times that of IVL.

The nonconsecutive nature of patient accrual to the study was not due to any selection, but rather to the following factors: 1) a slow start due to overcoming the inertia of traditional methods of patient management, 2) logistical problems of scheduling, patient transport, and so forth, and 3) occasional unavailability of the IVL staging procedure when one of the authors (R.W.B.) was out of town.

The DL diagrams judged inferior to those obtained by IVL were drawn by a chief resident in seven cases and by an attending physician in four, raising the possible criticism that DLs might have fared better if more of them had been performed by a more experienced surgeon. Yet, even if a higher number of attending physician DL diagrams had been included in the study, and if they had proven to be more accurate, the result would have been to increase the number of diagram pairs judged to be equivalent, because none of the 11 IVL "winners" were judged to be "better, but still inaccurate." It also can be pointed out that by the time of residency completion, recent chief residents in the Loyola University Department of Otolaryngology have been listed as primary surgeon for an average of 465 direct laryngoscopies. Finally, it should be noted that a sense of competition with IVL was fostered during each DL, in order to stimulate a "best effort."

The ability to obtain tissue for diagnosis is central to the justification of IVL. In this study, biopsy was attempted only ten times (tissue already obtained or about to be obtained at DL made office biopsy superfluous in 29 cases), but it was successful in nine of these ten attempts. Although the author performing indirect biopsies in this study (R.W.B.) prefers the forceps method in routine circumstances, it can be argued that use of a fiberscope with biopsy channel would be the method of choice for small, superficial vocal fold lesions, and, in practiced hands, could increase the rate of success even in "difficult" patients and lesions.

It could be argued that the overall goal of eliminating preliminary DL and biopsy also could be served by DL and biopsy with frozen section as a first step of definitive surgery in patients who have signed permission for all conceivable procedures suggested by mirror/fiberoptic examination. This approach rarely might be necessary, but we do not feel that patients handled in this manner are adequately prepared for an emotion-charged operation such as total laryngectomy, or one that might disrupt the swallowing mechanism. Also, histopathologic states other than squamous cell carcinoma are notoriously difficult to diagnose on frozen section, and the rare patient with another tumor type (lymphoma, small cell carcinoma) for which the preferred treatment is nonsurgical could be misdiagnosed.

Direct laryngoscopy was judged superior to IVL for three of four pharyngeal wall tumors, because of the need to palpate such tumors as an important means of determining invasion of prevertebral fascia. Also, IVL may not be as naturally suited to tumor mapping in the pharynx as it is in other sites, because problems with secretions and pain/poor cooperation are frequent (although hypopharyngeal suctioning and manipulation, which became more vigorous as the study proceeded, add considerably to the versatility of IVL for pharyngeal wall tumors). However, the main surgical planning consideration for cancers of this site — namely, whether or not the larynx can be spared — often can be assessed well with IVL of pyriform and postcricoid areas.

Considering both the advantages and the disadvantages of IVL mentioned above, IVL with biopsy appears to be a viable alternative to the traditional use of DL and biopsy for staging purposes. On the basis of our results, the authors intend to incorporate IVL staging of suspected larynx and pharynx cancers, without DL other than that performed as the initial step of definitive surgery, as an option for selected patients, and to continue to assess the accuracy of the method.

For others interested in this approach there are some caveats. First, IVL for cancer staging must be aggressive, as described above, to be of value, and should be scheduled and approached more as a DL than a routine office visit. Experienced endoscopists must commit approximately 30 to 40 minutes to each such procedure. They must be able to elicit cooperation from the occasional patient with a strong gag reflex or a high degree of anxiety. They must be skilled in methods of topical anesthesia and technically able to examine indirectly and manipulate the structures of the hypopharynx, larynx, and upper trachea when necessary. With experience, all of the above skills are accessible to the highly motivated otolaryngologist, but others pursuing this course should formally assess their own relative accuracies of DL and IVL before diminishing the role of preliminary DL and biopsy in diagnosis and management of patients with suspected head and neck tumors.

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INTERNATIONAL CONFERENCE AND WORKSHOP
HEAD AND NECK CANCER REHABILITATION

An International Conference and Workshop on Head and Neck Cancer Rehabilitation will be held March 14-18, 1990, at the Ritz Carlton Hotel in Dearborn, Michigan. For further information, contact Department of Otolaryngology, Wayne State University, School of Medicine, 4201 St Antoine, 5E - UHC, Detroit, MI 48201; (313) 577-0804.

Ann Otol Rhinol Laryngol 98:1989

LONG-TERM RESULTS OF ETHMOID SURGERY

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This paper investigates the results of nonendoscopic intranasal ethmoid surgery on 146 patients who were followed up for 6 to 13 years. These patients are divided into four groups: 1) infection without allergy, 2) infection with allergy, 3) infection with polyps and no allergy, and 4) infection with polyps and allergy. These groups are evaluated as to the long-term results of surgical treatment with or without concurrent allergic desensitization. The great majority of patients benefited from the surgical treatment regardless of their allergic status. Postoperatively, the allergic patients had more subjective symptoms than those having only infection. A major conclusion was that the long-term benefit to the patient as a result of the operation performed by experienced hands does override the potential risks of ethmoid surgery.

KEY WORDS — allergy, ethmoid surgery, nonendoscopic intranasal procedures, polyps.

INTRODUCTION

Several authors have reported series on the results of ethmoid-sphenoethmoid surgery.[1-4] The purpose of this paper is to report on 346 consecutive nonendoscopic intranasal procedures performed on 185 allergic and nonallergic patients from 1976 through 1982. As a result of the time frame, a 6- to 13-year follow-up has been obtained on 146 of the 185 patients, who had 276 procedures. A large number of patients on whom at least a 6-year follow-up was unattainable are excluded. Thirty-nine patients who had a greater than 6-year follow-up but whose current status is unknown are not included.

SURGICAL INDICATIONS

Seventy-six of the 146 patients had polyps (hyperplastic sinusitis), while the remaining 70 had recurrent acute and/or chronic infectious disease as demonstrated by history, examination, and radiographic findings. Two patients who had infection and malignancy are not included in the study.

TECHNIQUE

These patients with few exceptions had their procedures under attended local anesthesia because of decreased blood loss and improved safety of the operation (Sogg, unpublished observations). Septal mobilization (septoplasty) was done preceding the nonendoscopic intranasal ethmoidectomy for improved middle meatal exposure.[5] The middle turbinate was preserved as a landmark whenever possible. The instruments employed are those associated with the "classic" intranasal ethmoidectomy. Dissection was started at the ethmoid bulla because of its constancy.[6] Following the dissection of the bulla, the anterior ethmoid was widened medially and laterally with a Kerison rongeur. The agger nasi cells, when present, were marsupialized and the anterior ethmoid cells dissected in a tactile manner when the surgeon was unable to work under direct vision. The dissection then was carried to the anterior wall of the sphenoid. The procedure was completed by dissection anteriorly along the fovea, lateral surface of the middle turbinate, and orbital plate. The sphenoid, when entered, had the opening made medially and inferiorly but above the area of the attachment of the posterior end of the middle turbinate to the posterior ethmoid (anterior sphenoid) wall. Sphenoid punches were used for removal of the anterior sphenoid wall. At the time these procedures were done (1976 to 1982) the ethmoids were packed routinely for 24 to 48 hours with bacitracin-impregnated Vaseline gauze — the time depending on the amount of intraoperative bleeding. Currently, patients are packed only when the bleeding exceeds 150 to 200 mL.

The technique employed in managing the allergic patients has been described by the author.[7]

METHODS

The results reported are on 146 consecutive patients operated on by the author from 1976 to 1982. Some of these patients, fortunately for follow-up purposes, have returned periodically with nonsinus problems. Others have been seen for recurrent or continuing ethmoid problems. Approximately 45 of these patients were seen for various amounts of time following surgery for management of their allergies. Thirteen patients are known to have been treated elsewhere for allergies.

The patients not seen as described above were contacted either by phone (by the author) or seen in follow-up and questioned about their symptoms and feelings regarding the long-term outcome of the surgery.

Presented at the meeting of the American Laryngological Association, San Francisco, April 1-2, 1989.

REPRINTS — Alan Sogg, MD, 21100 Southgate Park, Cleveland, OH 44137.

RESULTS OF ETHMOID SURGERY BY PATIENT GROUP

			Results				
Group	Definition	No. of Patients	No Recurrence of Disease	Recurrent Infection	Persistent Allergy Symptoms	Recurrent Polyps	Revisions
1	Nonpolypoid infections without allergy	53	38	15	—	—	1
2	Nonpolypoid infections with allergy	17	13	4	4*	—	3
3	Polypoid disease without allergy	35	29	6	—	6*	5
4	Polypoid disease with allergy	41	21	14	14*	6	6†

*Same patients who had recurrent infections.

†Six revisions in five patients.

RESULTS

According to disorders, the patients were divided into four groups (see Table), for which the results were as follows.

Group 1. Nonpolypoid infections without allergy accounted for a total of 53 patients, of whom 38 have remained asymptomatic. Fifteen patients have experienced from one to five proven recurrent ethmoid infections over the time frame of the study. One required revision surgery in this group.

Group 2. Seventeen patients had nonpolypoid infections with allergy, of whom 13 have remained without infection, leaving four with recurrent symptoms of allergy and/or infection. Three required revision surgery.

Group 3. Polypoid disease without allergy affected 35 patients, of whom 29 have remained free of pus and polyps. Six in the group have regrown polyps. Five required revision surgery.

Group 4. Forty-one patients had polypoid disease with allergy, of whom 21 have remained free of pus, polyps, and allergy symptoms. Fourteen have continuing problems with allergy or infection, and six have regrown polyps. Six revisions have been performed on five of these patients.

COMMENT

Upon review, the relatively large number of patients that did not return for extended postoperative examinations was unexpected — this in spite of follow-up care being stressed as a preventive measure for avoiding recurrent problems. (The use of a computer to flag these patients for phoning appears to help reduce this situation.) The pleasant aspect of this group was that the majority, when contacted, said in effect, "I felt fine and didn't see any need to return." A few failed to return because of inconvenience (transportation, employment, distance, etc).

Fifteen revision procedures were required. That is not to say that some of the patients "lost" to follow-up did not seek treatment elsewhere. Unfortunately, this number is not known.

The most challenging patients in this and other series are those with nasal polyps, particularly if they are also allergic. If these polyps occurred as a result of infection only, the success rate was 83%; however, if allergies were also present, whether known at the time of surgery or even years later, the cure rate (group 4) as evidenced by absence of pus, polyps, and allergy symptoms was 51%. Thirty-four percent had continuing allergy symptoms, while 15% regrew polyps. An interesting additional result of this study was that postoperatively, 30 of 45 patients in groups 2 and 4 stopped or decided against starting allergic desensitization. None of these patients regrew polyps, but all did have "mild" allergy symptoms with or without asthma. None felt the need for desensitization; however, the relationship of allergy to chronic sinusitis is a recognized clinical entity[8] and is demonstrated further in this study.

There were no major complications. One patient had postoperative bleeding requiring packing, and 1% to 2% of the patients developed periorbital swelling and ecchymoses as a result of exposure or removal of periorbital fat. There was no morbidity such as diplopia, ocular fixation, or other sequelae in this group. This author does not feel that removal of periorbital fat is a complication in itself, unless it goes unrecognized and further intraorbital damage occurs.

CONCLUSIONS

1. The long-term results of intranasal ethmoid surgery reported in this and other papers warrant the potential risks of the procedure in experienced hands.
2. The possibility of recurrent problems or persistent disease does exist and should be recognized by the physician and patient.
3. The allergic patient, with or without polyps, is more difficult to manage and even perform a diagnosis on, and hence these cases require more effort and time from both patient and physician.
4. Follow-up visits are recommended as a way of recognizing recurrent problems as early as possible.

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NIH THERAPEUTIC STUDY OF FOLLICULAR THYROID CARCINOMA

The National Institutes of Health request the cooperation of physicians in referring patients with pure follicular thyroid cancer for a randomized clinical trial that will investigate the effectiveness of radiosensitizing agents in enhancing radioiodine therapy. Patients should have had primary thyroid surgery, without additional therapy for recurrences, and meet one of the following criteria: 1) age 40 years or older at the time of diagnosis with either primary tumor greater than 3 cm, regional lymph node metastases, extensive tumor capsule penetration, or extensive angioinvasion; or 2) any age with either tumor penetration into surrounding tissues or metastases outside of the neck.

All medical care expenses at NIH will be covered by the government except for transportation costs. Physicians will be informed regularly about the status of their patients and will continue to provide long-term care for them. Please write or telephone Dr Kenneth B. Ain or Dr Jacob Robbins, Bldg 10, Rm 8N315, National Institutes of Health, Bethesda, MD 20892; (301) 496-2831 or (301) 496-5761.

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CONGENITAL SUBGLOTTIC STENOSIS: THE ELLIPTICAL CRICOID CARTILAGE

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Various malformations of the cricoid cartilage produce congenital subglottic stenosis. The elliptical cricoid cartilage first was demonstrated histopathologically in horizontal sections of six postmortem specimens and now has been identified clinically in ten patients. The clinical diagnosis of the elliptical cricoid cartilage, suggested by anteroposterior soft tissue neck films, is confirmed at direct laryngoscopy. Delineation of the precise location, extent, and histopathology of subglottic stenosis provides the basis for rational management.

KEY WORDS — congenital laryngeal anomalies, elliptical cricoid cartilage, laryngeal stenosis, subglottic stenosis.

INTRODUCTION

Congenital subglottic stenosis is one of the most common causes of airway obstruction in infants and children[1] and is the most common laryngotracheal anomaly necessitating tracheotomy in infants under 1 year of age.[2]

Subglottic stenosis refers to a narrowing or stricture of the subglottic larynx, the subglottis being defined as the region extending from the insertion of the conus elasticus into the vocal folds to the inferior margin of the cricoid cartilage.[3] This basic definition is reviewed here since authors in all specialties are not uniformly precise in their description of subglottic lesions. Laryngotracheal stenoses or pure tracheal stenoses sometimes are grouped with discussions of subglottic stenosis.

Subglottic stenosis may be classified in three ways: 1) etiologic (congenital or acquired), 2) clinical/anatomic (hard or soft), and 3) histopathologic.[4] Subglottic stenosis is considered congenital when there is no other apparent cause for the stenosis such as long-term intubation.[4] Patients considered to have acquired subglottic stenosis due to previous intubation sometimes may have a congenital component as well. The clinical diagnosis is made by direct laryngoscopy and palpation of the stenotic area to determine if it is hard or soft.

The Table outlines the histopathologic classification of subglottic stenosis. A hard stenosis may be cartilaginous or fibrous. Cartilaginous subglottic stenosis is usually congenital and cannot be dilated. In the case of fibrous subglottic stenosis there is typically a history of intubation or some other form of laryngeal trauma. This form of subglottic stenosis can be dilated but tends to restenose. The soft stenoses are usually acquired and most often represent either granulation tissue or submucosal mucous gland hyperplasia. Combinations of the above, along with subglottic cysts,[5] are also possible.

The particular cartilaginous deformity of the cricoid cartilage discussed herein is a congenital one: the elliptical cricoid cartilage. An ellipse is defined as a closed plane curve generated by a point moving in such a way that the sum of its distances from two fixed points remains constant. As used here, the term is meant to describe a cricoid cartilage generally elliptical in shape in which the anterior-posterior diameter of the lumen is greater than the transverse diameter.

The elliptical cricoid cartilage first was described in 1979 by Tucker et al.[2] They recognized the anomaly by studying the horizontal preparations of infant larynges rather than coronal sections. Coronal sections of the larynx, ideal for the study of

HISTOPATHOLOGIC CLASSIFICATION OF SUBGLOTTIC STENOSIS

- Cartilaginous stenosis (usually congenital)
  - Cricoid cartilage deformity
    - Normal shape, small size
    - Abnormal shape
      - Large anterior or posterior lamina
      - Generalized thickening
      - Elliptical shape
      - Cleft: partial, occult (submucosal), complete
      - Flattened shape
      - Other, including acquired lesions
  - Trapped first tracheal ring
- Soft tissue stenosis (usually acquired)
  - Submucosal mucous gland hyperplasia
  - Submucosal cysts
  - Submucosal fibrosis
  - Granulation tissue

From the Division of Pediatric Otolaryngology, The Children's Memorial Hospital, and the Department of Otolaryngology-Head and Neck Surgery, Northwestern University Medical School, Chicago (Holinger), and the Department of Otolaryngology, Long Island College Hospital, Brooklyn, New York (Oppenheimer). Supported in part by a grant from the Lillian Shedd Wells Foundation through its funding of the Laryngeal Development Laboratory at The Children's Memorial Hospital, Chicago.

Presented at the meeting of the American Laryngological Association, San Francisco, April 1-2, 1989.

REPRINTS — Lauren D. Holinger, MD, The Children's Memorial Hospital, 2300 Children's Plaza, Chicago, IL 60614.

laryngeal cancer, were used almost exclusively until the horizontal technique was initiated. This major new approach led to the recognition of the elliptical cricoid cartilage and other cricoid cartilage anomalies. Since the original description, the elliptical cricoid cartilage has been documented histopathologically in six postmortem specimens and observed clinically in ten patients.

METHODS

Sixteen cases of elliptical cricoid cartilage were identified at The Children's Memorial Hospital in Chicago between 1975 and 1987.

Six cases were recognized at postmortem examination and comprise all the elliptical cricoid cartilages in the collection of the Laryngeal Development Laboratory in Chicago. These six whole organ laryngeal specimens were obtained at autopsy and preserved and processed according to the protocol developed by Tucker. They were embedded in pyroxylin (Parlodion) and sectioned at 28 μm in the horizontal plane from top to bottom, with every 20th section mounted as part of a tracer series.[5]

Ten of the cases were diagnosed clinically by endoscopy. Endoscopic examination was accomplished with the patient under general inhalation anesthesia, during spontaneous ventilation without an endotracheal tube. Direct visualization of the larynx was made first with a standard laryngoscope tip in the vallecula. A 0° Hopkins rod-lens telescope was used to examine the posterior glottis and tracheobronchial tree. The subglottic region was inspected with an anterior commissure laryngoscope by separating the vocal folds gently with the tip. This important maneuver provides an optimal view of the subglottis and posterior glottis, so the shape of the inferior half of the cricoid cartilage can be determined and a posterior laryngeal cleft ruled out. A side-slide laryngoscope placed in the vallecula facilitates palpation of the subglottis and the posterior glottis. A 3-mm bronchoscope should pass through the larynx of a newborn. A gentle attempt to pass a dilator through a hard stenosis helps to determine whether the lesion is a cartilaginous deformity or a fibrous cicatricial stenosis. Passing a bronchoscope or dilator of known size provides a precise, objective measure of the laryngeal lumen.

CASE REPORT

A boy 2 years 9 months of age and weighing 2.5 kg had been delivered with forceps at 35 weeks' gestation. He was intubated half an hour after birth to relieve severe respiratory distress. The endotracheal tube was removed when he was 10 days old. He did well until 7 months of age, when he was reintubated for a severe episode of croup. He was diagnosed as having subglottic stenosis at another institution, where he underwent laser procedures at 8 and 9 months of age. After another episode of croup at 33 months of age, a tracheotomy was done.

Radiographs demonstrated a subglottic stenosis with an hourglass deformity of the airway (Fig 1A). Direct laryngoscopy revealed an elliptical cricoid cartilage (Fig 1B,C). The lumen at the level of the cricoid cartilage was 8 to 9 mm in the anteroposterior plane but only 1 mm in the transverse plane. Interestingly, when laryngotracheal reconstruction was accomplished some time later, it was determined that he also had a fusion of the first and second tracheal rings. He subsequently was decannulated and has done well since.

RESULTS

All ten clinical cases of elliptical cricoid cartilage were diagnosed endoscopically. Age at diagnosis ranged from 2 to 8 months, 6 months being the mean. All patients had preliminary radiographs that showed subglottic stenosis. Eight of the ten were boys. Six had required intubation immediately postpartum.

Only one child who had an elliptical cricoid cartilage did not require tracheotomy. Eight of the nine tracheotomies were done several months following extubation because of severe upper airway obstruction symptoms. Seven of the nine tracheotomized patients were decannulated 2 to 4 years posttracheotomy. Only one of these required laryngotracheal reconstruction.

Only three of ten patients had congenital anomalies of other systems. One had central hypoventilation syndrome with a congenital heart disorder; another, Down syndrome with an atrial septal defect and hydrocephalus. A third child had CHARGE association. Three patients also had a trapped first tracheal ring.[2]

Three of the six infants whose larynges were histologically examined had associated anomalies. Two had tracheal agenesis, one of whom also had a patent ductus arteriosus and an incomplete posterior laryngeal cleft (Fig 2A). The other had anomalies of the ribs, kidney, and heart (a ventricular septal defect) (Fig 2B). One other had an occult posterior laryngeal cleft and submucosal cysts (Fig 2C).

DISCUSSION

Congenital subglottic stenosis is a clinical endoscopic diagnosis encompassing a variety of conditions that narrow the subglottic airway. The diameter of the lumen at the level of the cricoid cartilage in a normal newborn is 5 to 6 mm. Anything less than 3 mm is considered a severe stenosis.[6] P. H. Holinger et al[3] described an abnormally shaped cricoid cartilage causing subglottic stenosis as early as 1954. Morimitsu et al[7] reported six studies describing abnormalities of the cricoid cartilage in

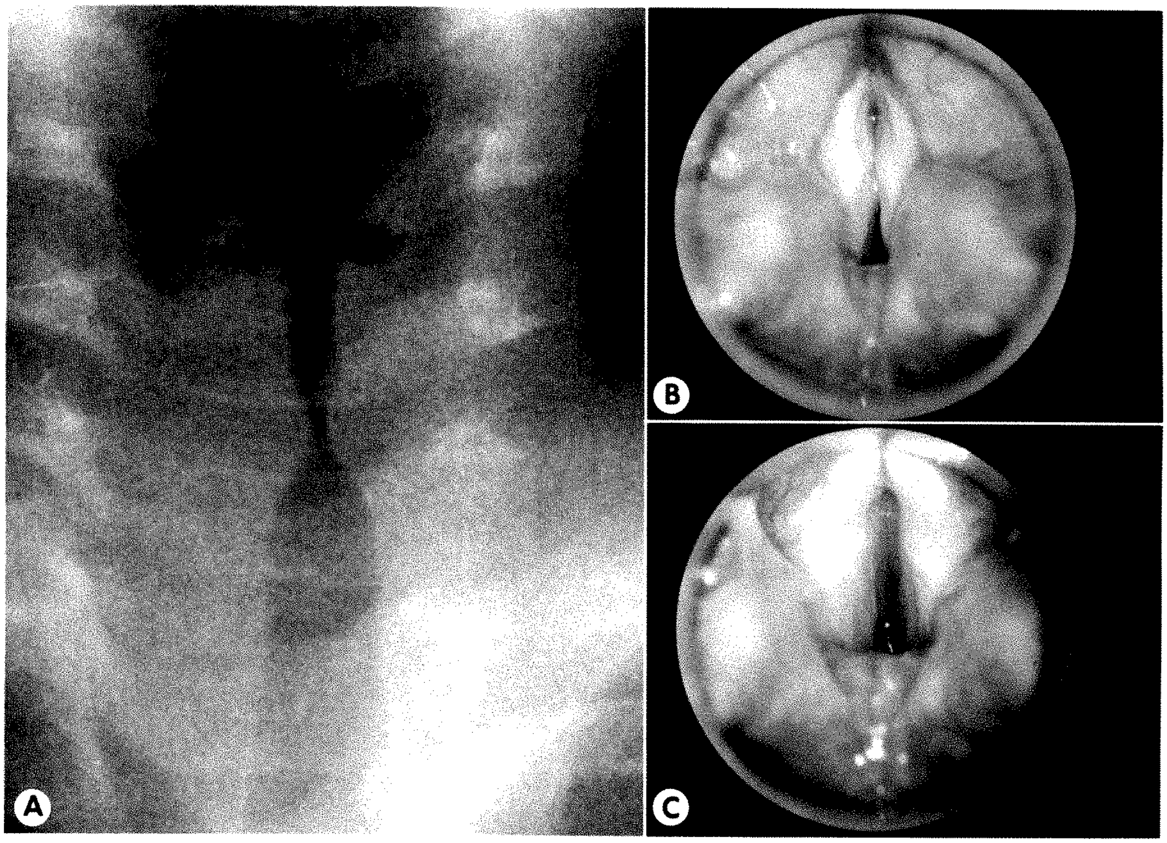

Fig 1. Case report. A) Anteroposterior radiograph of neck demonstrating "hourglass" deformity of airway due to elliptical cricoid cartilage. B) Endoscopic photograph at direct laryngoscopy demonstrating apparently normal larynx. C) Attempt to advance laryngoscope through vocal folds is prevented by severe narrowing of immediate subglottic larynx due to elliptical cricoid cartilage.

1981. Fearon and Cotton[8] categorized three different forms of subglottic stenosis based on the cricoid cartilage: 1) normal shape but small size, 2) normal shape, with submucosal fibrosis, and 3) abnormal shape. Holinger[9] further detailed classification of subglottic stenosis according to histopathology (see Table).

The anteroposterior diameter of the elliptical cricoid cartilage is greater than the transverse diameter (Fig 2D). This produces a mechanical obstruction, whether or not there are concomitant soft tissue abnormalities. However, in patients with inflammation, edema, or intubation trauma, soft tissue can cause additional narrowing. Stridor, recurrent or persistent croup, and the other manifestations of upper airway obstruction are therefore typical symptoms of the elliptical cricoid cartilage.

The diagnosis can be made with a good quality radiograph of the neck. Schlesinger and Tucker[10] described four cases of subglottic stenosis due to elliptical cricoid cartilage and pointed out that on the plain anteroposterior neck film the elliptical cricoid cartilage creates a specific hourglass deformity of the subglottic airway (Fig 1A).

The cricoid cartilage may well be the most prominent structure in the midline of the child's neck below the hyoid bone.[6] The abnormal shape of an elliptical cricoid cartilage is thought to be the result of a defect in the embryologic development of the larynx.[7,11,12] The actual mechanism is controversial. According to Schlesinger and Tucker,[10] Frazer theorizes that the stenosis is due to a failure of adequate recannulation of the larynx at the 9-week embryo stage. Walander[13] postulates that the larynx develops from a solid outgrowth of epithelial tissue from the pharynx and that arrests of laryngeal development at different stages may lead to stenosis at different levels.

The congenital origin of the stenosis is evidenced further by twin premature babies treated at The Children's Memorial Hospital in Chicago who had congenital subglottic stenosis with an elliptical cricoid cartilage. Two postmortem specimens had associated laryngeal anomalies (including posterior laryngeal clefts), additional evidence of a defect in embryologic development. In cases of occult posterior cleft larynx, the soft tissue is intact posteriorly but the cartilage is not.[14] This anomaly is present in six specimens in the Laryngeal Development Laboratory, but has been recognized by the senior author (L.D.H.) only once clinically. It may be more common, but endoscopic findings are extremely subtle.

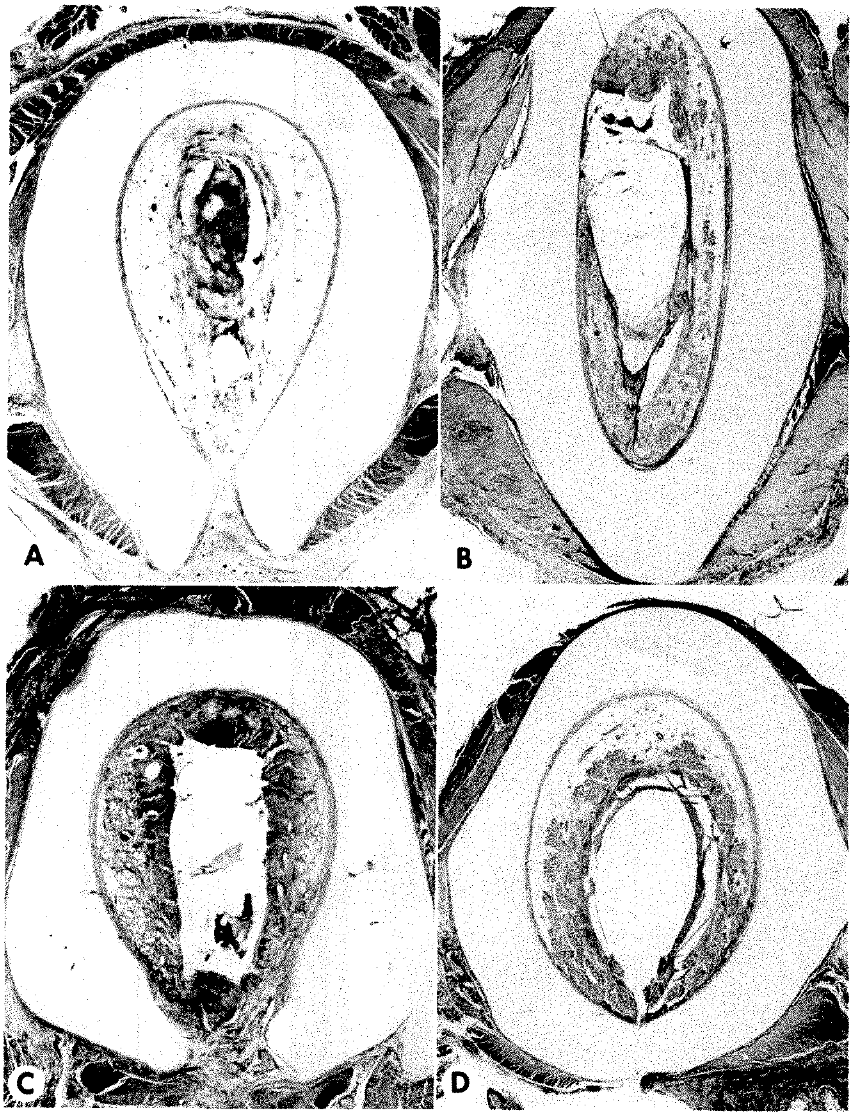

Fig 2. Horizontal sections. A,B) Two infants with tracheal agenesis. Both died within 48 hours of birth. A) Section through caudal end of cricoid cartilage. Larynx was partially cleft. Section demonstrates elliptical shape and submucous posterior cleft. B) Grossly distorted elliptical cricoid cartilage. C) Elliptical cricoid cartilage and lumen with occult submucous posterior cleft. Soft tissue is intact, but cartilage is cleft. Lumen also is compromised by submucous gland hyperplasia and microscopic ductal cysts (probably acquired). D) Elliptical cricoid cartilage and lumen. There is artifact posteriorly (bottom) where larynx was opened at time of autopsy.

The importance of precisely defining the nature of each case of subglottic stenosis is that the appropriate treatment cannot be planned without this information. Cartilaginous stenoses are usually not amenable to dilation, although with time, the infant may eventually outgrow the problem.[4] Careful endoscopy following an initial episode of croup in a child under 1 year of age should lead to earlier diagnosis. Since croup rarely occurs before 1 year of age, endoscopy should be undertaken in any child under 12 months who has a severe episode of croup. The procedure is deferred for at least 2 weeks following such an episode to minimize the potential for complications.

The high incidence of tracheotomy (90%) in this series suggests that only the most severe cases of elliptical cricoid cartilage are being recognized. The diagnosis may be made more frequently with a heightened awareness of the condition and careful attention to endoscopic technique.

Eight of the nine patients with tracheotomies were decannulated without surgical intervention — certainly evidence that in cases of elliptical cricoid cartilage, the larynx grows and the airway improves. It is not clear from our data whether or not the anterior cricoid split might be a useful operation for severe upper airway obstruction due to elliptical cricoid cartilage. Certainly the carbon dioxide laser, which can be used to treat soft tissue subglottic stenosis, is not used to treat the elliptical cricoid cartilage or any cricoid cartilage deformity.[9]

CONCLUSION

With careful attention to endoscopic technique, elliptical cricoid cartilage as a specific type of congenital subglottic stenosis may be diagnosed with increasing frequency. As with all types of laryngotracheal stenoses, the treatment of elliptical cricoid cartilage depends on the precise type, location, and severity of stenosis.

ACKNOWLEDGMENTS — We thank Geri Miseska for the preparation of the manuscript, Alina Roszel for the preparation of the laryngeal specimens, and Joseph Ficner for photography of the laryngeal sections.

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RED BLOOD CELL SCAN IN CAVERNOUS HEMANGIOMA OF THE LARYNX

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Cavernous hemangioma of the larynx is an uncommon, difficult-to-diagnose vascular tumor for which there is no significant imaging literature to date. The possibility of improved diagnosis through RBC scanning might obviate injudicious biopsy and potential hemorrhage within the airway. Utilizing the radionuclide RBC scan, which labels the patient's own RBCs initially with cold pyrophosphate, and subsequently with technetium 99m as pertechnetate, we have identified successfully four patients with cavernous hemangioma of the larynx. All presented with a supraglottic mass involving at least the aryepiglottic fold and arytenoid region unilaterally. This report describes our satisfactory diagnostic imaging experience with the radionuclide RBC scan and suggests both its imaging specificity and its role in the management of this lesion.

KEY WORDS — blood pooling, cavernous hemangioma, physiologic imaging, radionuclide imaging, red blood cell scan.

INTRODUCTION

Cavernous hemangioma is an unusual vascular lesion that occurs in the liver, skeletal muscle, and some structures of the head and neck. Though uncommon in the head and neck, it has a predilection for the parotid gland, tongue, and larynx. There has been much in the literature within the past half decade to identify the radionuclide RBC scan as the imaging method of choice for the identification of cavernous hemangioma in the liver; this is a clinical situation in which a policy of nonintervention has proven appropriate. However, nothing has appeared in the head and neck imaging literature about applying the technique to better identify this lesion in this region.

Our recent experience with four cavernous hemangiomas of the larynx suggests that the RBC scan may be capable of specifically identifying this lesion. Further, the effective identification of this vascular lesion allows for a hands-off policy with annual photographic follow-up of these lesions, which are notoriously difficult to ablate, and treatment of which often results in both deformity and functional derangement. If clinical assessment, augmented by definitive RBC scan imaging, allows specific diagnosis, then it is possible to formulate a more reasonable management approach to these patients.

A variety of imaging techniques have been suggested in a general sense for the identification of vascular lesions in general and cavernous hemangioma in particular. These imaging modalities include plain radiography, computed tomography, and now magnetic resonance imaging. Angiography, including screening assessment with digital intravenous subtraction angiography, is also used, obviously. This report identifies our experience with radionuclide scanning utilizing technetium 99m (Tc 99m)-labeled RBC scanning in four patients with cavernous hemangioma of the larynx. These patients also were imaged comparatively with other imaging modalities that lack the specificity of the RBC scan.

It was obvious that the radionuclide study takes full advantage of the unique blood pooling that occurs in cavernous hemangioma, as the capillary bed opens into dilated venous sinusoids prior to entering the venous circulation. Thus, blood pools and "percolates" uniquely in a way that lends itself specifically to RBC scanning and thus the identification of the cavernous hemangioma. Hence, the positive image of the RBC scan derives its specificity from physiologic, rather than anatomic, considerations.

METHODS AND MATERIALS

Over 6 years ago, the first patient at Mount Sinai with a possible cavernous hemangioma of the larynx was identified clinically. At that time, it was determined to advance a policy of nonintervention combined with annual observation and photography. Further, it was decided to assess this lesion by RBC scanning to determine its specificity in supporting the diagnosis. Thereafter, the senior author (A.M.N.) decided to continue to assess cavernous hemangiomas of the head and neck, further hoping to identify them prospectively by RBC scanning. Ultimately, three additional cases were identified in the larynx clinically and by RBC scan. Optimal im-

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TABLE 1. PATIENT SUMMARY

Case	Age (yr)	Sex	Symptoms	RBC Scan	Other Imaging	Annual Photo	Biopsy/Laser Intervention	Years of Follow-Up	Change
1	53	M	–	+	Dynamic computed tomographic scan	+	–	6	–
2	33	F	+	+	Computed tomography	+	Laser	6	–
3	52	F	Larynx –, tongue +	+*	Soft tissue lateral radiograph, ultrasound, magnetic resonance imaging, digital subtraction angiogram	+	–	4	?
4	74	M	+	+	Computed tomography	+	Biopsy	3	–

*With single photon emission computed tomography (SPECT).

aging therefore was clinically directed, with supervision of each imaging study by one of the authors (J.C.K.). Further, all patients agreed to be followed annually over time and to undergo other imaging modalities when suggested. The results of this study and the follow-up of these four patients over 6, 6, 4, and 3 years, respectively, is reported.

CASE REPORTS

The comparative clinical features of these four patients are summarized in Table 1, which shows whether the patient had symptoms (hoarseness), whether the patient had a positive RBC scan, other imaging studies that were carried out, whether there was controlled clinical assessment with annual photography and videotaping, instances of biopsy/laser intervention, the number of years of follow-up, and the presence of any change.

Case 1. A 53-year-old man, initially seen for vertigo, was referred for a second opinion concerning a vascular mass involving the left aryepiglottic fold. On telescopic assessment a 2-cm, lobulated, bluish vascular mass was seen occupying the lower portion of the left aryepiglottic fold, extending onto the arytenoid cartilage, and prolapsing into the medial aspect of the left pyriform sinus. A dynamic CT scan (Fig 1A) revealed a mass of rapidly enhancing vascularity involving the left supraglottis in the region of the aryepiglottic fold. The relative vascular uptake of this lesion was compared to that of the common carotid artery and the internal jugular vein, as well as that of the avascular contralateral sternomastoid muscle. Thus, the lesion was initially identified as vascular, but its specificity was not recorded. An RBC scan (Fig 1B) yielded results that were interpreted, on delayed imaging, as having the blood pool characteristics of a cavernous hemangioma. This patient has been followed for more than 6 years with annual photography and videotaping. He has no symptoms, and the mass remains unchanged.

Case 2. A 33-year-old woman presented with several months of hoarseness as her only complaint. On otolaryngologic examination, she had what appeared to be a large hemangioma involving the left supraglottis, including the ventricular band and aryepiglottic fold. It extended into the medial

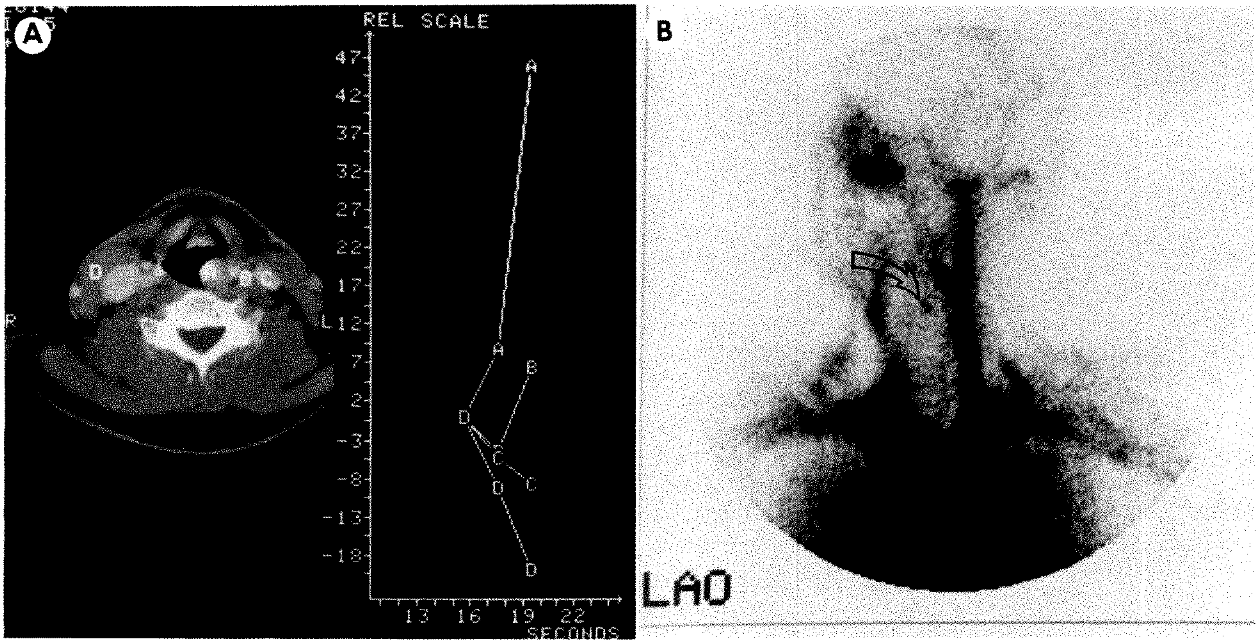

Fig 1. (Case 1) A) Dynamic computed tomographic scan demonstrating vascularity of left aryepiglottic fold lesion (A) as compared with common carotid artery (B), internal jugular vein (C), and avascular contralateral sternomastoid muscle (D). B) Left anterior oblique view of RBC scan, in delayed pool study, demonstrating focal image of laryngeal cavernous hemangioma (arrow).

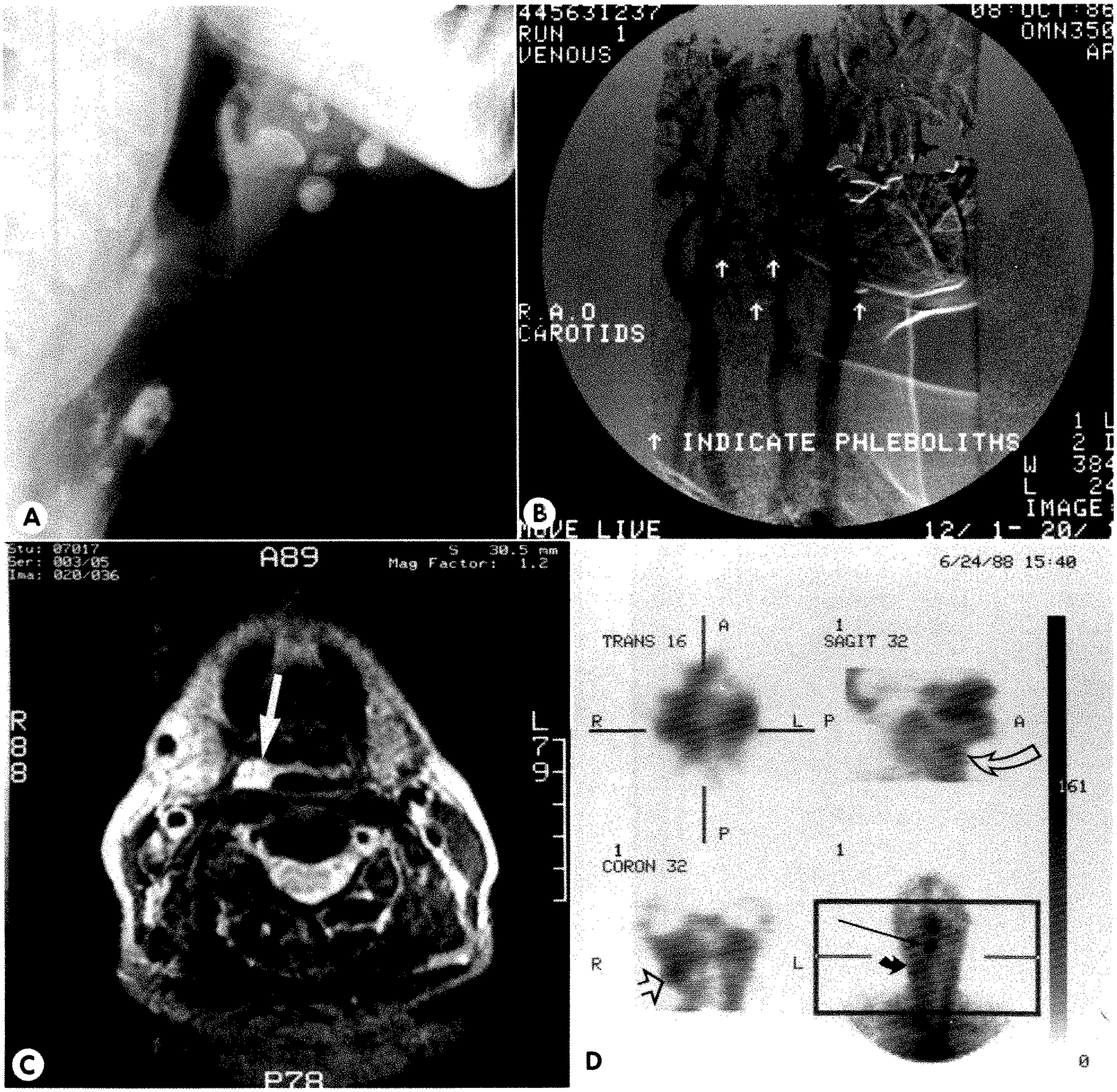

Fig 2. (Case 3) A) Soft tissue lateral radiograph demonstrating numerous phleboliths. B) Right anterior oblique view of arterial phase of intravenous digital subtraction angiogram demonstrating phleboliths (arrows), but no vascular imaging of lesion. Lesion also failed to fill on capillary and venous phase images. C) T2-weighted magnetic resonance image giving bright signal from supraglottic lesion at level of epiglottis (arrow). D) RBC scan imaged in planar display in lower right corner of composite image. Long thin arrow — delayed pool imaging of lingual portion of cavernous hemangioma; heavy curved arrow — laryngeal and adjacent deep cervical portion of same cavernous hemangioma. In lower left hand corner of composite image, coronal single photon emission computed tomography display demonstrates deep cervical portion of cavernous hemangioma (hollow arrow). Axial reconstruction is shown in upper left corner, and sagittal reconstruction is shown in upper right corner. Hollow curved arrow — laryngeal component of cavernous hemangioma.

aspect of the pyriform sinus. Vocal cord mobility was normal.

A conventional contrast-enhanced CT scan demonstrated a large left supraglottic mass with aryepiglottic fold involvement. The lesion deformed the left pyriform sinus. There was no contrast enhancement identified on early imaging with bolus injection. The initial impression was not that of cavernous hemangioma. However, a Tc 99m RBC scan demonstrated activity in the region of the left supraglottis on the early blood pool images, and this activity was greatly increased on the late blood pool imaging beyond 1½ hours. The imaging diagnosis was cavernous hemangioma.

A portion of the supraglottic mass was removed by laser to reduce encroachment of the supraglottic mass on the glottis, but it had little functional effect on the voice. The lesion has remained unchanged

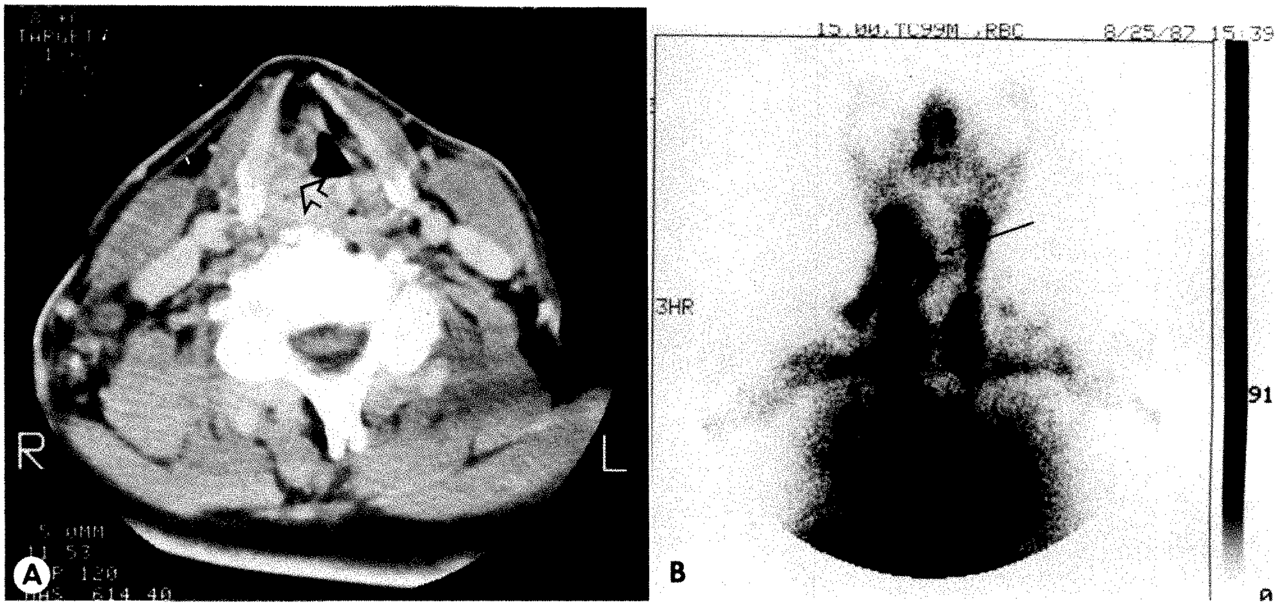

Fig 3. (Case 4) A) Computed tomograph demonstrating paralaryngeal mass that does not enhance with contrast. Its posterior extension is indicated by arrow. Scan is nondiagnostic. B) Anterior planar image of RBC scan of larynx demonstrating typical vascular configuration of cavernous hemangioma (arrow). Delayed pool phenomenon is critical to its identification.

over 6 years and has been photographed annually.

Case 3. A 52-year-old woman presented with a 40-year history of swelling of the right side of the tongue that intermittently became increasingly engorged, but always regressed. At times, this lingual swelling would interfere with tongue mobility and speech, but there was never a history of dyspnea, dysphagia, or voice change. On examination, a large, purplish, submucosal vascular lesion was visible, involving the right half of the tongue. The lesion extended inferiorly into the larynx and involved the right aryepiglottic fold and the right half of the epiglottis. Calcified phleboliths could be palpated in the submandibular and supralaryngeal regions.

A soft tissue lateral radiograph of the neck demonstrated several calified phleboliths in the plane of the tongue and the supraglottis (Fig 2A). A digital subtraction angiogram, utilizing an intravenous technique, failed to identify a vascular lesion in the arterial, capillary, or venous phases. Only the phleboliths were identified (Fig 2B), but the vascular nature of the lesion remained undemonstrated. An MRI study (Fig 2C) demonstrated findings compatible with cavernous hemangioma on the T1-weighted, intermediate, and T2-weighted images. An especially bright signal was noted on the late T2-weighted image, compatible with the diagnosis of cavernous hemangioma. A Tc 99m–labeled RBC scan with single photon emission computed tomography (SPECT) revealed increased blood pooling over time in the right half of the tongue and supraglottis (Fig 2D) diagnostic of cavernous hemangioma.

The patient has been followed annually with photographs and videotaping over 4 years, and the laryngeal lesion remains unchanged; she questions whether her tongue lesion has altered, but photographs do not clearly suggest a change.

Case 4. A 74-year-old man, a nonsmoker, was referred for evaluation of hoarseness. On examination, there was an apparent vascular fullness of the posterior portion of the right aryepiglottic fold, but it did not have the purplish clinical blush seen in the three previous patients. A CT scan of the larynx (Fig 3A) demonstrated a large right paralaryngeal mass that did not enhance with intravenous contrast. This involved the supraglottis and the posterior portion of the aryepiglottic fold. Both the clinical appearance and the CT appearance were compatible with a variety of lesions other than cavernous hemangioma. A Tc 99m–labeled RBC scan demonstrated delayed pooling that gradually intensified over 3 hours of imaging — a pattern consistent with cavernous hemangioma. Because of the atypical clinical findings, and yet the rather specific RBC scan findings, microlaryngoscopy and biopsy were carried out. The pathologic findings were completely compatible with cavernous hemangioma. The patient has now been followed with annual photography over the past 3 years, and the lesion remains unchanged.

DISCUSSION

Hemangiomas are benign neoplasms of blood vessels that can occur anywhere in the body, but have a predilection for hepatic, musculoskeletal, and head and neck sites. They can be subclassified into capillary, cavernous, and "mixed" types based on histology, although some argue that the distinction is artificial.[1]

TABLE 2. IMAGING MODALITIES IN CAVERNOUS HEMANGIOMA OF LARYNX

	Morphologic	*Physiologic*
RBC scan	+	+ + + +
RBC scan with single photon emission computed tomography (SPECT)	+ +	+ + + +
Computed tomography with contrast enhancement	+ + +	+
Dynamic computed tomographic scan	+ + +	+ + +
Magnetic resonance imaging	+ + + +	+ +
Ultrasound	+	+
Conventional radiographs	+	0
Digital subtraction angiogram	+ + +	+ + +

Pluses show relative value of modalities.

Cavernous hemangiomas of the head and neck can occur in the facial and skull bones, soft tissues of the orbit, salivary glands, or anywhere beneath the mucosa of the upper aerodigestive tract. Histologically, these lesions comprise tangles of thin-walled vessels, sometimes dilated to huge size, in which there may be sludged blood. These huge vascular spaces predispose to spontaneous thrombosis and subsequent calcification and the development of calcific lesions called phleboliths. These are entirely characteristic of cavernous hemangioma and can be recognized clinically (case 3) and on radiography. These vessels are separated by a scanty connective tissue that may resemble erectile tissue.[1]

Depending upon their location, cavernous hemangiomas of the head and neck may be either asymptomatic or symptomatic, with symptoms of laryngeal cavernous hemangiomas ranging from mild dysphagia to hoarseness to airway obstruction.

While preoperative diagnosis on clinical grounds is often possible, especially with superficial mucosal lesions, atypical and deep lesions may prove a diagnostic dilemma (case 4). It is imperative that the attending surgeon discover whether a lesion is a cavernous hemangioma or other vascular lesion or a vascular-mimicking tumor before formulating a therapeutic plan. Cavernous hemangioma is a benign lesion, and it is essential to avoid surgical misadventure, as these lesions have been reported to bleed to the point of exsanguination after conventional biopsy, surgery, or dentistry.[2] Further, surgical treatment, even with the laser, often leads to deformity and dysfunction.

How then should a clinician proceed to investigate a lesion suggestive of cavernous hemangioma? We feel that the Tc 99m–labeled RBC scan provides unique anatomic and physiologic information unobtainable with other imaging modalities, and hence has an important role in the diagnosis of this entity.

Cavernous hemangiomas have a distinct appearance on Tc 99m RBC scanning that follows from a direct understanding of both the anatomy of the lesion and the physiology of the labeled erythrocyte. These lesions contain dilated vessels through which pooled blood "percolates" at a much slower velocity than through surrounding tissues. We used the "in vivo" method of labeling RBCs, in which stannous pyrophosphate is injected as a reducing agent and is followed shortly thereafter by a further in vivo injection of Tc 99m pertechnetate. The technetium binds to the beta chain of the hemoglobin molecule without disrupting the integrity of the cell. In addition, we give a single oral dose, 400 mg, of potassium perchlorate; the perchlorate competitively binds to technetium, which then is blocked from entering the thyroid and salivary glands. These glands otherwise would accumulate label and make the distinction between lesions and background noise more difficult. This labeling method reveals that under ideal conditions, 90% of the injected label is present in the blood flow 30 to 120 minutes after injection, of which at least 95% is bound to RBCs.[2] In practice the amount of label available is dependent upon a number of factors, such as concurrent illness, drug use, and renal function. Thus, the labeled RBCs are available for a considerable length of time within the blood pool, leading to the classic appearance of a cavernous hemangioma upon sequential scans.

A study performed immediately after injecting the label (the "flow study") will show little or no increased activity in the involved area. An early blood pool study, done several minutes after injection, may show the beginning of accumulation of label at the involved site; however, accumulation is greatest after waiting 90 to 120 minutes (the "late pool" study), at which time accumulation at the site of involvement is significantly greater than in the surrounding tissues. This appearance, ie, poor perfusion and slow filling of the tumor, has been termed the "perfusion–blood pool mismatch" and is characteristic of the cavernous hemangioma.[2] The addition of SPECT to the planar scintigraphy studies, as demonstrated in case 3 of our series, increases the contrast resolution of the images and may allow clearer definition of the size of the lesion.[3] Indeed, recent reports of cavernous hemangiomas of the liver reveal that SPECT images may be much more accurate at detecting small (less than 2 cm) lesions.[4,5]

Other imaging modalities are identified comparatively in Table 2. Conventional radiographs do not define the anatomy of the hemangioma, and certainly do not reveal physiology. However, the finding of phleboliths is diagnostic. The CT scan may not demonstrate significant contrast enhancement in the early imaging study, as explained under the "perfusion–blood pool mismatch" concept of the RBC scan above. Thus, CT with contrast enhancement may not demonstrate the lesion, and dynamic CT also may be misleading. Equally, conventional angiography, or screening examination with digital subtraction and intravenous injection, may fail to perfuse the lesion in the early arterial, capillary, and venous imaging. However, digital subtraction angiography is given high credit for both morphologic and physiologic imaging because it eliminates other vascular lesions — a critical aspect of differential diagnosis.

Computed tomography often can delineate anatomic boundaries of the tumor, but is not specific for the lesion. In cavernous hemangiomas, CT is reported as having wide ranges of densities with respect to surrounding tissues, and thus can provide confusing data.[2,6] Further, in RBC scanning, whole labeled RBCs are used as an intravascular agent, whereas CT contrast can diffuse rapidly into the extracellular matrix through gaps in the endothelium of the vessels of the tumor. Also, the contrast is cleared rapidly by renal mechanisms, and only 35% is available in the bloodstream 2 hours postinjection; thus, the classic late filling picture seen in cavernous hemangioma will be missed.[2] For the same reasons, conventional arteriography may not always show the true nature of the lesion, as the dye may be excreted before the late pool filling has had a chance to occur, although one report several years ago claimed success at diagnosing cavernous hemangiomas of the neck and tongue by internal jugular and subclavian venography.[7]

Magnetic resonance imaging may prove useful in the diagnosis of these lesions. In liver hemangiomas, the tumors appear markedly hyperintense compared with skeletal muscle at long TR and TE intervals; further, the slow blood pool may predispose to increased signal intensity on T2-weighted images. The role of MRI in these lesions is in evolution, and further data are needed before definitive recommendations can be made.[6,8] Further, the high signal intensity on the T2-weighted image is characteristic of many other lesions as well.

Finally, ultrasound may demonstrate the apparent septate nature of superficial lesions, but does not image the larynx well, especially when the thyroid cartilage is calcified. Its value therefore is limited.

In summary, as shown by the four cases discussed above, Tc 99m–labeled RBC scanning provides important anatomic and physiologic identification of patients with cavernous hemangioma. It is suggested that this may be the definitive imaging modality upon which clinical decision-making can be based.

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HYDROXYLAPATITE FOR LARYNGOTRACHEAL FRAMEWORK RECONSTRUCTION

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Hydroxylapatite plates and rings were employed for reconstruction of the laryngotracheal framework in 12 patients. The cause of the framework defect was surgery for stenosis in nine cases and removal of malignancy in the other three. The trough method associated with a two-stage procedure was tolerated in all 12 cases. Hydroxylapatite plates or rings were used to reconstruct the framework during the second stage. The implant was well taken in all cases, without any infection or rejection. Nine of the 12 cases resulted in excellent airways.

KEY WORDS — hydroxylapatite, laryngotracheal framework, laryngotracheal reconstruction.

Autogenous tissues including the costal, thyroid, and epiglottic cartilages and hyoid bone have been shown to be excellent materials for reconstruction of the laryngotracheal framework.[1-8] The only notable disadvantage of this option is the additional surgery required for the donor site. Any potential disadvantage associated with donor site surgery is avoided when artificial materials are used.[9] Hydroxylapatite (HA) and other types of ceramics have been employed successfully to reconstruct the middle ear ossicles, external auditory canal, mandible, orbital wall, and frontal bone[10-15]; however, they have not been described in laryngotracheal framework surgery. This paper describes the use of HA in reconstructing the laryngotracheal framework.

MATERIAL AND TECHNIQUE

The technique described here evolved over the course of a 3-year period involving 12 patients. Initially, HA plates were fabricated by Asahi Optical Co, Tokyo. The size of the plate was adjusted to the size of the framework defect of each individual patient. The plates were perforated with small holes that could be used for stabilization sutures. Custom design for each patient meant considerable time delay between the design of the plate by the surgeon and its completion by the fabricating company. Thus, subsequently we designed two sizes of HA rings that simulated the size and shape of tracheal rings (Fig 1). The larger ring was 20 mm in diameter, and the smaller one, 16 mm. Both rings were 1.5 mm thick and 5 mm long. Similar to the normal anatomic configuration, the fabricated ring was incomplete for about 60° or one sixth of its entire circumference. Small indentations (approximately 1 mm wide) were made on the superior and inferior borders of the ring. The indentations were made every 60° and were used to facilitate stabilizing the ring against the neighboring tissues with sutures. At the time of the operation the prefabricated rings were trimmed to adapt to the size of the framework defect present in the patient.

Surgery using the HA plate or ring was conducted in two stages. The exact procedure used during the first stage was contingent upon the problem presented. In cases of carcinomatous invasion of the laryngotracheal framework, the involved portion of the framework was removed along with the original neoplasm, and the cervical skin was sutured to the laryngotracheal mucosa to construct a trough. In cases of stenosis of the larynx and/or trachea, the lumen was widened by splitting laryngeal and/or tracheal cartilage and removing scar tissue and granulation tissue. The laryngeal and/or tracheal cavity was entirely lined with the remaining normal mucosa, advanced cervical skin, and/or a skin or mucosa graft. A trough was made at the location in which the stenosis had existed. A straight plastic tube or T-tube was inserted in the trough.

During the second stage both types of cases were treated similarly. A medially based skin flap was designed along one side of the trough. On the other side, an incision was made near the edge of the trough. The flap was elevated, rotated, and sutured to the skin near the opposite edge to form the anterior wall lining of the larynx and/or trachea. Occasionally, medially based skin flaps were made along both sides of the trough and were rotated and sutured to each other. Then HA plates or rings were placed on the rotated skin flap and securely sutured to it. The wound was covered with either a rotation or an advanced skin flap. Figures 2 and 3 show photographs taken during surgery.

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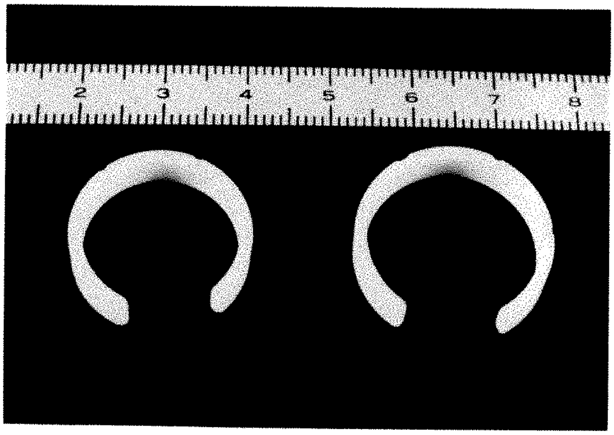

Fig 1. Hydroxylapatite rings. Ruler is in centimeters.

REVIEW OF CASES

During the 3-year period from 1985 to 1987, HA was used for reconstruction of the laryngotracheal framework in 12 patients. The Table summarizes the cause and site of the framework defect along with a list of any concomitant problems, the type and size of the HA implant, and the surgical outcome for each of the seven male and five female patients. Their ages ranged from 4 to 70 years. The cause of framework defect was surgery for stenosis in nine cases, thyroid cancer in two, and recurrent glottic cancer in one. In the nine cases of stenosis, the stenosis resulted from prolonged endotracheal intubation in four, inadequate tracheostomy or posttracheostomy complication in four, and hemilaryngectomy in one. The degree and extent of stenosis varied. Five patients had near-total obstruction, whereas four had half to three-quarters obstruction. The framework defect was located at the larynx in one patient, at the trachea in six, and at both larynx and trachea in five.

Two patients had severe brain damage (patients 6 and 12 in the Table) that caused unconsciousness in one case and mental retardation associated with paralysis of extremities in the other. Both patients were bedridden. One patient had severe cerebral palsy (patient 11) and was nonambulatory.

In this series of 12 patients HA plates were used in the first five patients and HA rings were employed in the subsequent seven. With the exception of one patient requiring two plates, all of the plate patients had one HA plate. In the HA ring patients, one required three rings, three needed two rings, and a single ring was used in the other three. The size of the HA plate varied from 9 x 14 mm to 30 x 20 mm, as shown in the Table. The large HA rings were used for adults, and the small HA rings for children.

In general, the laryngeal and/or tracheal opening was completely closed at the time of the reconstructive surgery. In two patients (patients 6 and 11), however, it was partially closed. In patient 6, who had severe brain damage, adequate expectoration function could not be assured and a means of airway control was necessitated. Therefore, we decided to keep a tracheostoma at the lower end of the tracheal opening. Patient 11 had tracheal stenosis extending from the cervical trachea to the cervicothoracic junction. At the time of the first stage of surgery, the innominate artery was found to be in front of the trachea at the level of the upper edge of the sternum. Therefore, the trachea could not be widened surgically to the normal size at the cervicothoracic junction. The stenosis was eliminated surgically in the cervical trachea. During the second stage of surgery, the upper portion of the tracheal opening was closed, but the lower end, at which the size of the tracheal lumen was narrower than the normal size, was kept open. In patient 12, the tra-

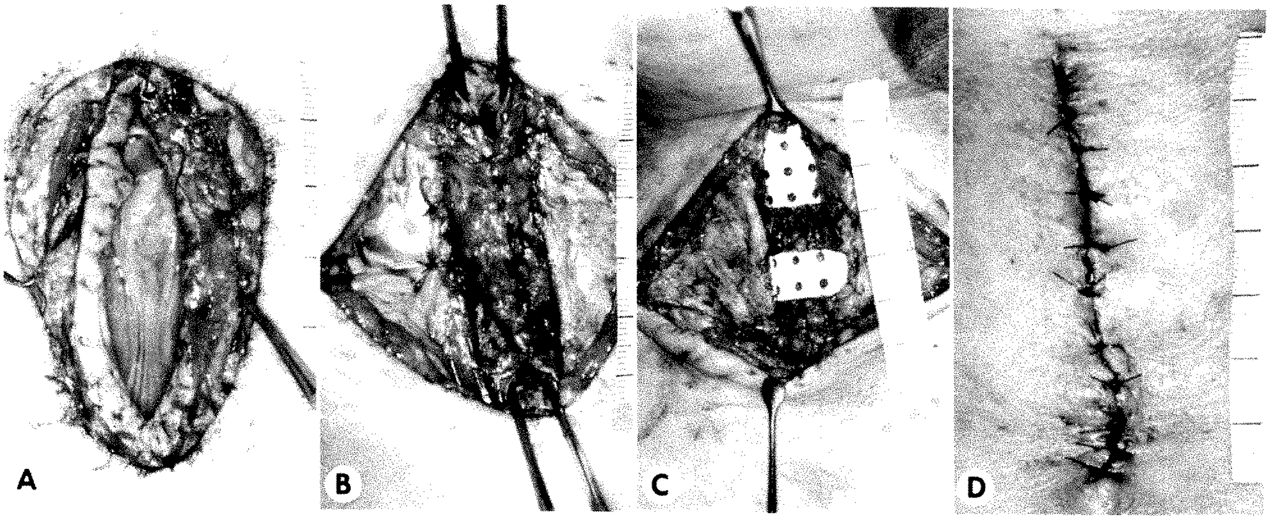

Fig 2. Photographic illustration of operative procedure employing hydroxylapatite plates for reconstruction of laryngotracheal framework defects. Rulers are in centimeters. A) Skin incision around trough. Flaps have been designed bilaterally. B) Skin flaps have been rotated and are being sutured to each other. C) Hydroxylapatite plates are placed. D) View at end of operation.

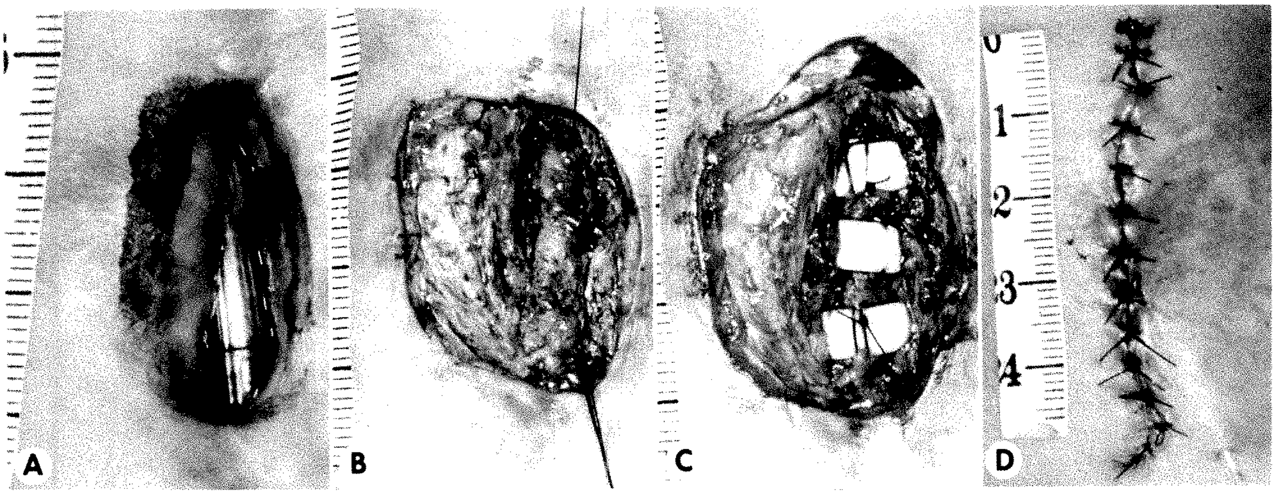

Fig 3. Photographic illustration of surgery employing hydroxylapatite rings for reconstruction of laryngotracheal framework defects. Rulers are in centimeters. A) Design of skin incision. B) Skin flap has been rotated and sutured. C) Hydroxylapatite rings are placed. D) View at end of operation.

chea was partially reopened shortly after surgery because the patient developed apnea.

Results of the HA plate and ring implantation were generally positive. The implanted HA plates and rings were well tolerated in all cases without any infection or rejection. An excellent airway was obtained in nine of the 12 patients. The duration of follow-up ranged from 14 to 40 months. In patient 6, in whom reconstruction of three fourths of the tracheal ring had been necessary, the HA rings tilted postoperatively. The tilted rings narrowed the reconstructed tracheal lumen to some extent and reduced the airway. Patient 12 died of intercurrent disease 4 months after surgery.

For the purpose of illustrating the details of the procedures, two cases are described. One is a case of framework defect caused by surgery for carcinoma, and the other is a case of laryngotracheal stenosis.

Patient 3 was a 60-year-old woman who underwent total thyroidectomy and bilateral neck and paratracheal dissections for T4N3M0 carcinoma of the thyroid gland on Jan 29, 1985. The anterior and left tracheal walls were removed at the first to third tracheal rings because of carcinomatous invasion. A trough was constructed at the tracheal opening by suturing of the tracheal mucosa to the skin. The postoperative course was uneventful. On Oct 17, 1985, the tracheal wall was reconstructed. The size of the tracheal opening was 29 x 10 mm. Medially based skin flaps were made along the trough bilaterally, rotated, and sutured to each other. An HA plate was placed on the rotated skin flaps and sutured to it. The wound was closed with a rotation skin flap. Three years 4 months postoperatively the patient had an excellent airway.

SUMMARY OF 12 CASES TREATED WITH HYDROXYLAPATITE FOR CORRECTION OF LARYNGOTRACHEAL FRAMEWORK DEFECTS

Patient	*Age*	*Sex*	*Cause and Site of Framework Defect*	*Concomitant Problem(s)*	*Type and Size of Implant*	*Outcome (Length of Follow-Up)*
1	67	M	Surgery for thyroid cancer, LT	None	Plate, 30 x 20 mm	NM, EA (49 mo)
2	47	F	Surgery for stenosis, T	None	Plate, 18 x 15 mm	NM, EA (46 mo)
3	60	F	Surgery for thyroid cancer, T	None	Plate, 28 x 8 mm	NM, EA (40 mo)
4	36	M	Surgery for stenosis, T	None	Plate, 14 x 10 mm	NM, EA (38 mo)
5	59	F	Surgery for stenosis, LT	None	2 plates, 21 x 18 mm and 9 x 14 mm	NM, EA (36 mo)
6	24	F	Surgery for stenosis, T	Brain damage, unconsciousness	2 rings, d = 20 mm	Partial closure, rings tilted (22 mo)
7	57	M	Surgery for stenosis, T	None	Ring, d = 20 mm	NM, EA (27 mo)
8	70	M	Surgery for stenosis, L	None	Ring, d = 20 mm	NM, EA (22 mo)
9	4	M	Surgery for stenosis, LT	None	Ring, d = 16 mm	NM, EA (22 mo)
10	56	M	Surgery for recurrent glottic cancer, LT	None	2 rings, d = 20 mm	NM, EA (14 mo)
11	30	F	Surgery for stenosis, T	Cerebral palsy	2 rings, d = 20 mm	Partial closure, NM (14 mo)
12	10	M	Surgery for stenosis, LT	Brain damage, mental retardation, paralysis of extremities	3 rings, d = 16 mm	Trachea partly reopened for apnea, died of intercurrent disease at 4 mo

L — larynx, T — trachea, d — diameter, NM — no morbidity, EA — excellent airway.

Patient 5 was a 59-year-old woman. On June 23, 1984, she was involved in a traffic accident that caused severe trauma of the chest and abdomen, and a femur fracture. She was treated at another medical center and was intubated for 28 days. Following extubation, she developed increasing dyspnea and had a tracheostomy on August 5. She was kept cannulated while she was treated for the chest, abdominal, and femur injuries. On April 30, 1985, she was referred to Kurume University Hospital for correction of her airway problem. A near-total obstruction was found at the subglottis and the upper portion of the trachea. On May 13, an open reduction was conducted. Following a midline cervical skin incision, the lower portion of the thyroid cartilage, the entire cricoid cartilage, and the upper tracheal rings were sectioned at the midline down to the level of the tracheostoma. The exposed area revealed that the subglottis and the upper portion of the trachea were nearly totally obstructed. The obstructive scar tissue was removed. The cricoid lamina also was sectioned at the midline and the bilateral laminar halves were separated, widening the posterior portion of the larynx. A composite nasal septum graft was placed between the separated cricoid laminar halves. The laryngeal and tracheal mucosa was sutured to the cervical skin anteriorly to construct a trough. A T-tube was inserted in the laryngotracheal lumen. The postoperative course was uneventful. The T-tube was removed 6 months later. In order to ensure the existence and maintenance of an adequate airway, the laryngotracheal trough was closed initially by means of adhesive tape. The patient was followed for 4 months and did not develop breathing difficulties. Consequently, on Feb 21, 1986, the 48 x 7-mm laryngotracheal trough was closed surgically. Two HA plates were used to reconstruct the anterior wall of the subglottis and trachea. The postoperative course was uneventful, and the excellent airway remains intact.

COMMENTS

The results of the present study suggest that HA can be a good alternative material in reconstruction of the laryngotracheal framework when the trough method is employed. The procedure reported here involves two stages. We are not able to determine whether or not HA can be employed for one-stage procedures, because we have had no direct experience of its use in these. The trough method has been conducted in our hospital primarily for the following reasons: it is rarely contraindicated, it allows surgeons to monitor the state of wound healing and patency of the laryngotracheal lumen, and it therefore permits relatively safe determination of adequate timing for subsequent closure. The disadvantage of the trough method is the fact that it calls for an additional surgical procedure to close the trough. This could well be balanced by the need for surgery at the donor site for procedures using autogenous tissue in some selected patients.

Autogenous tissues including the costal cartilage, epiglottis, and hyoid bone have proved to be excellent materials for reconstruction of the laryngotracheal framework. Basically, they do not cause immunologic rejection or foreign body response. We, too, have employed autogenous cartilages, including the costal and septal cartilages. The results have been excellent. The only disadvantage with autogenous tissues is the fact that they call for an additional procedure for the donor tissue.

Originally, HA was developed as a hard tissue prosthetic for bone.[16] When it is applied to bone, it becomes directly bonded to it by what may prove to be natural bone-cementing mechanisms. No local or systemic toxicity, inflammatory or foreign body response, or development of intervening fibrous tissue between bone and implant takes place. This is a very intriguing biologic feature for an implant for bone replacement. When HA is implanted in soft tissues, it becomes tightly adherent to neighboring tissues with connective tissue. However, no bone or osteoid tissue forms around HA.[17] This indicates that HA can be a good implantation material for extraosseous supporting tissues.

The use of HA for a one-stage reconstruction awaits further studies. We believe that implanted HA plates or rings cannot be exposed in the laryngeal and tracheal lumens and should be totally covered by living tissue. This is difficult to accomplish with current techniques in a one-stage reconstruction procedure and is likely to be the greatest technical difficulty to overcome.

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THE SIXTH WORLD CONGRESS FOR BRONCHOLOGY

The Sixth World Congress for Bronchology will be held October 18-20, 1989, in Tokyo, and October 20-22, 1989, in Kyoto, Japan. For further information, contact Dr Masayuki Niitsuma, Secretary General, 6th World Congress for Bronchology, Department of Surgery, Tokyo Medical College, 6-7-1 Nishishinjuku, Shinjuku-ku, Tokyo 160, Japan; telephone 03-342-6111.

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ACUTE AIRWAY OBSTRUCTION DUE TO NECROTIZING TRACHEOBRONCHIAL ASPERGILLOSIS IN IMMUNOCOMPROMISED PATIENTS: A NEW CLINICAL ENTITY

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Two immunocompromised patients with severe neutropenia developed acute airway obstruction due to *Aspergillus* mycetoma formation in the trachea and main bronchi. The mycetomas caused transmural necrosis of the airway. In one patient, the necrosis extended through the bronchus intermedius into the pulmonary artery, resulting in a fatal hemorrhage during bronchoscopy.

KEY WORDS — airway obstruction, *Aspergillus*, bone marrow transplantation, mycetoma, neutropenia.

Aspergillus has now emerged as the leading cause of death due to infectious fungal organisms in the immunocompromised host.[1] About 90% of the time, invasive aspergillosis involves the upper and lower respiratory tracts. Infections of the nose, paranasal sinuses,[2] mandible, larynx, tracheobronchial tree, and lung all have been encountered at the University of Minnesota Hospital and Clinic (UMHC). Infections of the ear[3] and the epiglottis[4] also have been reported. If untreated, invasive aspergillosis of the respiratory tract is almost always fatal.

It commonly was believed that intrathoracic aspergillosis in the immunocompromised host basically took two forms: invasive *Aspergillus* pneumonitis and *Aspergillus* bronchitis.

Aspergillus pneumonitis typically presents as dyspnea with a nonproductive cough and pleuritic chest pain in a febrile, neutropenic patient who has received multiple antibiotics for the empiric treatment of the fever. Plain chest films may show virtually any infiltrative pattern, and multiple peripheral sites are not uncommon. As the WBC count rises, the areas of invasive *Aspergillus* pneumonitis tend to become mycetomas.

Aspergillus bronchitis is a relatively indolent process that typically is diagnosed only at autopsy. It occurs in 5% to 10% of patients with disseminated aspergillosis. Pathologically, it is a superficial saprophytic growth of hyphae on the bronchial mucosa that, at worst, only superficially invades the mucosa.

Recently, a new distinct variant of *Aspergillus* bronchitis was described in a 15-year-old hemophiliac with acquired immune deficiency syndrome who developed severe neutropenia.[5] The clinical course was characterized by rapidly progressive dyspnea and wheezing. Autopsy disclosed that the distal trachea, right and left main bronchi, and many segmental bronchi were covered with a granular carpet of mycetomas. There was total obstruction of subsegmental bronchi and partial obstruction of larger bronchi. There was extensive necrosis of bronchial mucosa and frequent sites of transmural bronchial necrosis that extended into peribronchial tissue. The necrosis was due to tissue invasion by fungal elements.

This is the first reported case of necrotizing *Aspergillus* bronchitis. Recently, we encountered two similar cases of this new entity. This unique form of bronchitis merits attention because of its clinical and prognostic implications.

CASE REPORTS

Case 1. A 30-year-old man with chronic myelogenous leukemia was admitted to UMHC for bone marrow transplantation. Engraftment occurred, but he developed graft-versus-host disease, which itself is immunosuppressive, and he underwent further immunosuppression for its treatment (methylprednisolone).

He developed a cough and rapidly progressive shortness of breath at this time. Indirect laryngoscopy, while the patient was in respiratory extremis, disclosed a subglottic crust. An emergent tracheotomy under local anesthesia was performed. The tracheotomy was made purposely low, at the fifth tracheal ring. Removal of a portion of this ring revealed a nearly totally obstructing rubbery mass, and there was no space into which a tracheotomy tube or other artificial airway could be inserted. The mass could not be delivered through the tracheotomy site, and its consistency did not allow its rapid fragmentation. The mass finally was pushed superiorly through the glottis, and a tracheotomy tube was inserted.

The mass was recovered at laryngoscopy and proved to be a cylindrical *Aspergillus* mycetoma

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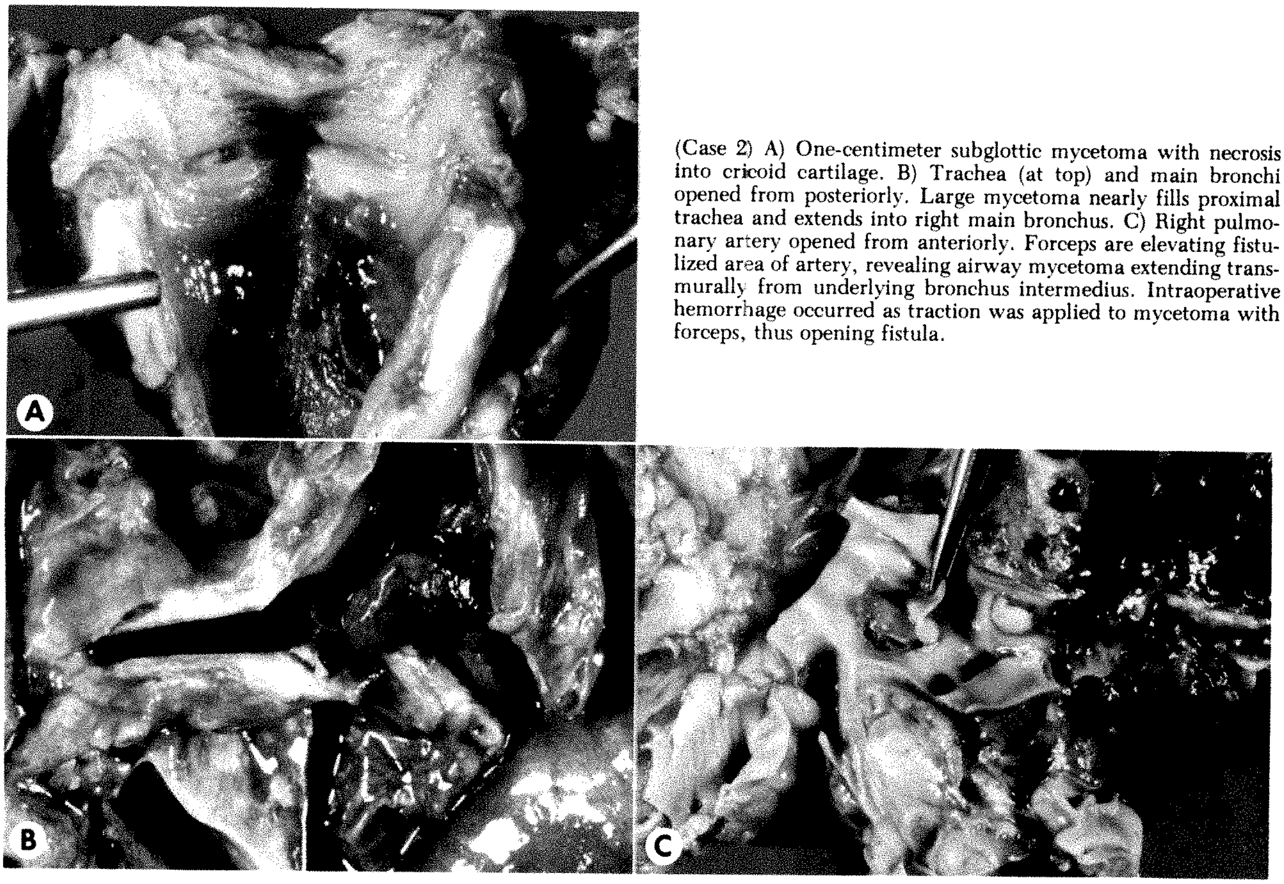
Presented at the meeting of the American Broncho-Esophagological Association, San Francisco, April 3-4, 1989.



(Case 2) A) One-centimeter subglottic mycetoma with necrosis into cricoid cartilage. B) Trachea (at top) and main bronchi opened from posteriorly. Large mycetoma nearly fills proximal trachea and extends into right main bronchus. C) Right pulmonary artery opened from anteriorly. Forceps are elevating fistulized area of artery, revealing airway mycetoma extending transmurally from underlying bronchus intermedius. Intraoperative hemorrhage occurred as traction was applied to mycetoma with forceps, thus opening fistula.

that measured 4 x 2 x 2 cm and originated from the subglottic area. The site of origin showed extensive necrosis of mucosa and cartilage. Bronchoscopy revealed other small mycetomas in the distal trachea and right main bronchus. The patient died 3 weeks later with a patent airway.

Case 2. A 21-year-old man with acute lymphoblastic leukemia was admitted to UMHC for chemotherapy. While severely neutropenic, with a WBC count of less than 500/mm^3, he developed a cough, and *Aspergillus fumigatus* was cultured from the sputum.

Sixteen days later, the WBC count had suddenly risen to 2,900/mm^3, and an indirect laryngoscopy revealed a 1-cm mycetoma in the right pyriform sinus. Two days later, the WBC count had risen to 4,400/mm^3, and he developed rapidly progressive dyspnea and shortness of breath.

Direct laryngoscopy now revealed that the pyriform sinus mycetoma had enlarged to 3 cm within 48 hours. A 1-cm fungal erosion with mycetoma formation was encountered in the subglottic area (see Figure, A). Bronchoscopy disclosed multiple small tracheal mycetomas and a massive, nearly totally obstructing mycetoma in the distal trachea and right main bronchus. An attempt to remove the large obstructing proximal mycetoma resulted in a profuse and uncontrollable hemorrhage that rapidly flooded the airway and caused a terminal cardiopulmonary arrest in the operating room.

Autopsy revealed no fungal elements in the lung by culture or light microscopy. The proximal trachea and right main bronchus were nearly filled with a mycetoma composed of fungal hyphae, fibrin, and leukocytes (see Figure, B). The mucosa was infarcted because of invasion by *Aspergillus* organisms. Transmural erosion occurred at the anterior bronchus intermedius into the right pulmonary artery (see Figure, C). A fistula between the bronchus intermedius and the right pulmonary artery was confirmed histologically.

DISCUSSION

Necrotizing tracheobronchial aspergillosis with mycetoma formation is a new clinical entity that now has been described in three patients. Several clinical aspects deserve special emphasis.

First, airway obstruction may be rapidly progressive because of rapidly enlarging mycetomas within the lumens of the larger airways.

Second, plain radiographs may be of little help to the endoscopist, since mycetomas may not be readily detectable on such studies. Furthermore, radiographs obtained a day or more prior to endoscopy may be misleading if the mycetomas are enlarging rapidly.

Third, the degree of airway obstruction can be worse than suspected on a clinical basis, since these patients usually have multiple other medical problems that can cause dyspnea and shortness of breath. The respiratory distress may be ascribed inappropriately to these other problems.

Fourth, the mycetomas tend to be multiple, and endoscopy is hazardous, since this situation is tantamount to multiple foreign bodies in the airway.

Fifth, and interestingly, symptoms of airway obstruction tend to develop and worsen as the WBC count improves in the neutropenic patient. Invasive aspergillosis in a severely neutropenic patient typically causes only a dry gangrene of mucosa. However, as immune capacities recover, particularly neutrophil function, *Aspergillus* can provoke its characteristic intense inflammatory response, and mycetoma formation can occur.[6]

The advanced stages of this disease are marked by intense mucosal necrosis that can be transmural. Our first patient demonstrated significant necrosis of the subglottic area. Our second patient demonstrated a fatal bronchoarterial fistula. Mineur et al[7] recently reported a case of an aspergilloma of the distal trachea and right main bronchus that had eroded into the esophagus, causing a clinical bronchoesophageal fistula, in a neutropenic cancer patient. This may qualify as a fourth case of necrotizing tracheobronchial aspergillosis.

The immunocompromised patients at risk for this disease are cancer patients in general, patients with leukemia or lymphoma undergoing chemotherapy, solid organ allograft recipients, bone marrow transplant recipients, and children with chronic granulomatous disease, a defect of neutrophil microbicidal function.

Based on the limited experience with this disease, some tentative recommendations may be made.

First, in a neutropenic patient with dyspnea, a sputum culture positive for *Aspergillus flavus* or *Aspergillus fumigatus* cannot be dismissed as a laboratory contaminant. Even if only a single colony is isolated, it can be indicative of *Aspergillus* pneumonitis or *Aspergillus* bronchitis.[8]

Second, a computed tomographic scan of the larynx, trachea, and chest should be obtained just prior to endoscopy if time permits. This may allow detection of mycetomas if they are present, and their number, size, and locations. Even a CT scan may be misleading, depending on the size of the interval between cuts.

Third, bronchoscopy should be performed initially only as a diagnostic measure. This would appear to be best performed in an awake patient who is ventilating spontaneously. Depending on the individual's experience and expertise, a flexible bronchoscope or a rigid bronchoscopic telescope alone should allow a rapid assessment of whether insertion of a larger rigid bronchoscope would precipitate airway obstruction.

Fourth, manipulation of mycetomas at areas in the airway adjacent to major vascular structures is fraught with danger, since transmural necrosis into these structures, with incipient fistula formation, may have occurred. If a fistula is suspected, especially with antecedent hemoptysis, it may be in the patient's best interest simply to do nothing. If a mycetoma presents on the posterior trachea, esophagoscopy would appear indicated to search for a tracheoesophageal fistula.

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USE OF CEFTAZIDIME FOR MALIGNANT EXTERNAL OTITIS

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During the past 2 years we have used ceftazidime (Fortaz), a third-generation cephalosporin, in the treatment of eight patients with progressive necrotizing "malignant" external otitis. Ceftazidime is very active against *Pseudomonas* species and provides penetration into the CSF. Our results suggest that this medication has several advantages over the previously recommended combinations of aminoglycosides and semisynthetic penicillins, including improved cure rate, lower toxicity, and simpler administration schedules. We review our experience with ceftazidime in the treatment of eight patients.

KEY WORDS — ceftazidime, malignant external otitis.

INTRODUCTION

Malignant external otitis (MEO), also known as necrotizing external otitis, is a progressive, destructive osteomyelitis of the skull base usually originating in the region of the bony external auditory canal (EAC). The infection probably begins as a typical external otitis due to *Pseudomonas aeruginosa*, which progresses to osseous involvement in individuals with abnormal leukocyte function, such as diabetics.

The treatment of this disorder has evolved from a surgical approach[1,2] to primary medical therapy with intravenous antipseudomonal antibiotics.[3,4] The standard agent is an aminoglycoside administered with a semisynthetic penicillin. Such therapy is complicated by the potential ototoxicity and nephrotoxicity of the aminoglycoside, administration of multiple intravenous drugs, high sodium content of the penicillin, and poor CSF penetration by the aminoglycoside.

Over the past several years, third generation cephalosporin antibiotics with good antipseudomonal activity have become available. Since they have shown success in osteomyelitis, the authors initiated a study to examine the effectiveness of one such cephalosporin, ceftazidime, in the treatment of MEO.[5]

DIAGNOSIS AND TREATMENT

All patients with the presumptive diagnosis of MEO were placed on the protocol outlined below after informed consent was obtained. Criteria for diagnosis included at least three of the following:

1. Persistent otalgia for longer than 1 week.
2. Persistent purulent otorrhea with granulation tissue for at least 1 week.
3. Diabetes mellitus, other immunocompromised state, or advanced age.
4. Cranial nerve dysfunction.

The treatment protocol initiated was as follows:

1. Patient admitted to hospital. Complete head and neck examination including microscopic examination of the EAC and tympanic membrane.
2. Aerobic culture and antibiotic sensitivity of the affected EAC.
3. Daily debridement of affected EAC as necessary. Instillation of topical antibiotic drops (Cortisporin otic solution four times daily).
4. Computed tomography of the temporal bones with axial and coronal cuts and contrast injection prior to treatment. Additional CT to be ordered as clinically indicated.
5. Gallium radionuclide scanning initially at 3 weeks and additional times if clinically indicated.
6. Intravenous ceftazidime 2 g every 8 hours for 4 to 6 weeks. Dosage lowered in case of impaired renal function.
7. Daily otoscopic examination.
8. Laboratory studies on admission: audiologic assessment (pure tone, speech, and impedance audiometry), complete blood cell count with differential, serum glucose, serum creatinine, electrolytes, liver function tests, urine analysis, chest radiography, electrocardiogram, platelet count, prothrombin time, partial thromboplastin time, serologic test for syphilis.
9. Laboratory tests during hospitalization: serum glucose weekly or more frequently if clinically indicated, serum creatinine and electrolytes weekly, complete blood cell count every 2 weeks, audiologic assessment.
10. Removal of granulation tissue from EAC for debridement purposes as well as for biopsy to exclude neoplasm.

CASE REPORTS

All patients presented with benign granulation tissue in the affected ear canal. Patient characteris-

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Presented at the meeting of the American Otological Society, Inc, San Francisco, April 2-3, 1989.

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PATIENT CHARACTERISTICS

Pt	*Age (yr)*	*Sex*	*Associated Medical Diagnosis*	*Creatinine (mg/dL)*	*Culture*	*Computed Tomography*	*Treatment*	*Outcome*
1	52	F	IDDM	0.8	*Pseudomonas aeruginosa*	Refused	Ceftazidime 2 g IV q8h for 6 wks	Resolved with no recurrence
2	72	M	None	1.0	*Pseudomonas aeruginosa*	STM in left ear	Tobramycin sulfate 100 mg, carbenicillin disodium 3 g IV q6h for 1 wk	Persistent granulation tissue
	72		None	1.0	Not performed	STM in left ear	Tobramycin sulfate 80 mg IV q8h, ticarcillin 3 g IV q6h for 4 wk	Resolved granulation; persistent pain in left ear
	73		Blindness in right eye, right vocal cord paralysis, ophthalmoplegia in right eye	0.8	No growth	Base of skull erosion	Ceftazidime 2 g IV q8h for 12 wk	Ophthalmoplegia resolved; persistent blindness in right eye, and right vocal paralysis; no further granulation tissue
3	81	M	Alzheimer's disease	1.2	*Staphylococcus aureus*	STM with no bone destruction in left ear	Ceftazidime 2 g IV q8h for 4 wk	Resolved with no recurrence
4	85	M	AODM	0.9	*Proteus mirabilis, Escherichia coli*	STM in EAC of left ear	Ceftazidime 2 g IV q8h for 5 wk	Resolved granulation; left facial paralysis 1 mo later
	85		AODM, facial paralysis	0.9	Not performed	Not performed	Ceftazidime 2 g IV q8h for 6 wk	Left facial nerve decompression with no improvement
	86		AODM, facial paralysis	0.9	*Pseudomonas aeruginosa*	STM in EAC with no bone destruction	Tobramycin sulfate 80 mg IV q8h plus piperacillin sodium 3 g IV q6h for 6 wk, ciprofloxacin 500 mg PO bid for 2 wk	Resolved granulation tissue; vertigo 2 mo later
	86		AODM, facial paralysis	0.9	Not performed	STM in EAC	Ceftazidime 2 g IV q8h for 3 wk	Persistent vertigo; no granulation tissue; peripheral vascular surgery
5	64	F	IDDM	3.6	*Pseudomonas aeruginosa*, enterococci	STM in EAC of right ear with bone erosion	Ceftazidime 1 g IV q8h for 6 wk	Resolved with no recurrence
6	52	F	AODM	0.9	*Pseudomonas aeruginosa, Proteus mirabilis*	STM in EAC of left ear	Ceftazidime 2 g IV q8h for 6 wk	Resolved with no recurrence, gallium scan negative at 2 wk
7	50	F	IDDM	0.9	*Pseudomonas aeruginosa*	STM in EAC of left ear	Ceftazidime 2 g IV q8h for 5 wk, ciprofloxacin 750 mg PO bid on discharge	Small amount of granulation on discharge, but no further recurrence
8	90	M	IDDM, right facial paralysis	1.2	*Pseudomonas aeruginosa*	STM in EAC of right ear with bone erosion	Ceftazidime 2 g IV q8h for 6 wk	Granulation resolved; persistent facial paralysis

IDDM — insulin-dependent diabetes mellitus, STM — soft tissue mass, AODM — adult-onset diabetes mellitus, EAC — external auditory canal.

tics, treatment, outcome, and complications are summarized in the Table. Two patients with complex courses are discussed in detail.

PATIENT 2

A 72-year-old man presented with several weeks of left-sided otalgia and otorrhea. A granular mass filled the left EAC. Biopsy revealed only granulation tissue. A CT scan of the temporal bones revealed a soft tissue mass in the left EAC with sclerosis of the left mastoid air cell system. His past medical history was unremarkable; the patient was not diabetic.

Oral trimethoprim-sulfamethoxazole and topical Cortisporin were administered without improvement. Six weeks after presentation he underwent a left exploratory tympanotomy and removal of granulation tissue from the middle ear. Postoperatively he received tobramycin sulfate and carbenicillin disodium. Over the subsequent 2 weeks, the patient complained of persistent otalgia. Culture of the left otorrhea revealed *Pseudomonas aeruginosa*.

The patient was admitted approximately 3 weeks after surgery because of the suspicion of MEO, even though he was not diabetic. Granulation tissue was present in the left ear; the tympanic membrane was intact. Tobramycin sulfate and ticarcillin were administered intravenously for 4 weeks, with resolution of the granulation tissue. Results of skin tests were positive for tuberculosis and mumps, thus demonstrating an intact T lymphocyte system.

Over the next 3 months, the patient complained of mild, deep-seated left otalgia. The physical examination findings remained normal.

Four months after discharge, the patient was admitted to a hospital in London, England, because of persistent left otalgia and neck pain. Because of an elevated sedimentation rate the diagnosis of temporal arteritis was made and the patient was treated with corticosteroids. Results of a temporal artery biopsy were normal. He developed right-sided palsies of nerves X, XI, and XII. Nasopharyngeal biopsy results were negative for tumor. A tympanostomy tube was inserted in the right ear.

He was readmitted to the London hospital 2 months later, still with the right-sided cranial nerve palsies. He was almost blind in the right eye. A CT scan showed a nasopharyngeal mass, and chest radiographs revealed a foreign body in the left lower lobe (an anesthesia stylette, probably dislodged during the previous nasopharyngoscopy). The foreign body was removed successfully by bronchoscopy. The patient returned to the United States directly from the hospital.

On presentation again to the New York Eye and Ear Infirmary, the patient was stuporous and complained of bilateral ear and neck pain. He was blind in the right eye. Granulation tissue was present in the right EAC. A tympanostomy tube was present in the right ear, which was dry. There was a right vocal cord paralysis, and cranial nerves III, IV, and VI were nonfunctional on the right.

The patient was given intravenous ceftazidime 2 g every 8 hours. The prednisone that had been prescribed in London was tapered gradually over the next several weeks. There was gradual improvement in his sensorium and extraocular motility; however, the right eye remained blind. Magnetic resonance imaging revealed no intracranial abnormality. A CT scan showed no base of skull destruction. The patient was discharged after 2.5 months of ceftazidime. The extraocular palsy resolved, but the blindness and right vocal cord paralysis persisted.

Comment. The patient had left-sided MEO that traversed the skull base to the right ear. Because the patient was not diabetic, the diagnosis was not suspected initially. Treatment with an aminoglycoside-penicillin combination improved the condition. In England, results of a workup for temporal arteritis, neoplasia, and Wegener's granulomatosis were negative. Prolonged treatment with ceftazidime permitted resolution, although some cranial nerve deficits persisted.

PATIENT 4

An 85-year-old man presented with persistent left ear drainage. Granulation tissue was present in the left EAC, and he was treated with Cortisporin and amoxicillin. After failing to improve he was admitted to the hospital 1 week later. Although he had no history of diabetes, he had an elevated fasting blood sugar. Biopsy of the EAC tissue revealed granulation tissue, and cultures showed *Proteus mirabilis* and *Escherichia coli*. A CT scan showed soft tissue in the left EAC and middle ear without bone destruction. He was treated with intravenous ceftazidime 2 g every 8 hours. Over the subsequent 5 weeks, the otalgia and granulation tissue resolved, and he was discharged.

The patient was admitted 1 month later because of sudden, total and complete left-sided facial paralysis. The left ear was otoscopically normal. Because of the possibility of neoplasia, a left facial nerve exploration was performed. Granulation tissue was found at the base of skull, extending into the fallopian canal through the stylomastoid foramen. The facial nerve was necrotic at the level of the foramen. Ceftazidime 2 g every 8 hours was administered intravenously for 6 weeks with no improvement of the facial paralysis.

Two months later, he was admitted because of left otalgia and granulation tissue in the left EAC. The left-sided facial paralysis was still present. A CT scan showed no bone destruction. Culture of the left EAC revealed *Pseudomonas aeruginosa* sensitive to ceftazidime. However, because of the previous failure of ceftazidime, the medical consultant urged the use of tobramycin sulfate and piperacillin sodium, which were given intravenously for 6 weeks. The granulation tissue resolved, but the facial paralysis persisted. On discharge, the patient received oral ciprofloxacin 500 mg twice a day.

Two months later the patient was readmitted because of vertigo. The left ear showed only cerumen; no granulation was present. The gallium scan showed increased activity in the left ear. Ceftazidime 2 g every 8 hours was given intravenously. After 3 weeks of intravenous antibiotics, the patient was transferred for femoral-popliteal bypass. His vertigo was felt to be secondary to aminoglycoside ototoxicity. When seen 3 months later, the EAC was normal. His left-sided facial paralysis persisted.

Comment. The indolent nature of MEO is exemplified by this patient. The sudden facial paralysis without concomitant EAC granulation prompted suspicion of neoplasia, but facial nerve exploration revealed only inflammation.

OVERALL RESULTS

Overall, ceftazidime treatment resulted in resolution of granulation tissue in the EAC in seven of eight patients, although two of these patients had a subsequent recurrence of the infection. Ceftazidime failed to resolve cranial neuropathy in the three patients affected, although ophthalmoplegia in one patient was relieved.

There were no deaths in this series of patients, all of whom have been followed for a minimum of 10 months.

DISCUSSION

Malignant external otitis is considered to be an osteomyelitis of the temporal bone that spreads through vascular channels to other parts of the base of the skull. From this point there is involvement of the cranial nerves at the foramina. Extension to the petrous apex allows advancement across the clivus along vascular or fascial planes to the opposite temporal bone.[6] Because of this mode of progression, surgical extirpation of the mucosally lined air cell system is usually of little benefit, as illustrated in the original description of Meltzer and Keleman.[1] This realization, coupled with pharmacologic advances, has made MEO primarily a medically treated disease.

Malignant external otitis is insidious, usually beginning as a common external otitis. However, in the setting of defective leukocyte migration and the microangiopathy frequently seen in diabetics,[7-9] this normally innocuous infection can progress to life-threatening sepsis. The *Pseudomonas* organism is able to invade poorly vascularized tissue through its elaboration of endotoxin and collagenase, to evade phagocytosis with its mucoid layer, and to escape pharmacologic destruction through its antibiotic resistance.

Malignant external otitis should be suspected in any patient with persistent otalgia and EAC granulation tissue. Concomitant diabetes mellitus, immunosuppression, debilitation, or advanced age also should raise suspicion of the diagnosis.[10] Malignant external otitis must be distinguished from cholesteatoma, neoplasms (squamous cell carcinoma, glomus tumors, clivus chordoma), histiocytosis, Wegener's granulomatosis, and temporal arteritis.[11] Computed tomography and/or MRI[12] are mandatory. Computed tomography will detect bone destruction and inflammatory involvement of the air cell system, temporomandibular joint, and skull base. Magnetic resonance imaging is very sensitive in delineating intracranial involvement. Technetium bone scans[13] identify osteoblastic activity during the active and healing phases of the disease, and gallium scans[14] are positive during the active inflammatory response. These imaging techniques aid in delineating the extent of bone and soft tissue involvement (CT, MRI, technetium) and in confirming the response to treatment (gallium).

Once the suspected diagnosis is strengthened by imaging techniques and biopsy and culture of the granulation tissue, local debridement or drainage of any purulent collection is performed. Medical therapy is initiated with the appropriate antipseudomonal agent. The physician has at his or her disposal quite an array of compounds, including aminoglycosides (gentamicin, tobramycin), carboxypenicillins and ureidopenicillins (carbenicillin disodium, ticarcillin disodium, piperacillin sodium), cephalosporins (ceftazidime), and quinolones (ciprofloxacin).[5] Conventional therapy has consisted of an aminoglycoside coupled with a penicillin for weeks[3] or months[15] until resolution.

Ceftazidime is a third generation, β-lactamase-resistant cephalosporin administered parenterally. It causes bacterial cell lysis and is bactericidal for *Pseudomonas aeruginosa* and other gram-negative organisms. It has demonstrated usefulness in the treatment of *Pseudomonas* osteomyelitis,[5] and its application to the treatment of MEO is an extension of this concept.

The current study demonstrated resolution of MEO-induced otalgia in all eight patients. Granulation tissue in the EAC was eliminated or greatly reduced in all patients. There were no drug-induced complications. Two patients had complex courses requiring several hospital admissions. One patient responded to ceftazidime after an initial failure with tobramycin and penicillins; the other had a recurrence of granulation after treatment with ceftazidime. This appears to be the only failure of ceftazidime in this series. Failure in this case is not surprising, since cranial nerve involvement is known to impart a poor prognosis, and extensive skull base involvement was identified surgically. These results are comparable to those in other recent series.[16]

Other investigators have reported using cephalosporin antipseudomonal agents to treat MEO. Haverkos et al[17] used moxalactam disodium in four patients. Two patients died soon after therapy. Myers et al[16] used the investigational drug cefsulodin to achieve a complete resolution in seven of 11 patients. Strauss[4] used a cephalosporin and ciprofloxacin with good results in a small series.

The success of ceftazidime in our patients is apparent, but treatment still requires the prolonged administration of a drug intravenously. Although this can be done in the home setting with close nursing supervision, these intensive services still require frequent physician monitoring to detect progression of disease, intravenous catheter complications, and drug toxicity. The recent availability of ciprofloxacin, an orally administered fluoroquinolone active against *Pseudomonas*, has opened up an alternative treatment protocol.[18] It may be possible in the future to obtain an initial response with intravenous ceftazidime and then add ciprofloxacin. The patient then could be discharged on a regimen of oral ciprofloxacin and monitored, thus eliminating the necessity for prolonged intravenous drug administration. Future investigations along this line show promise.

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CONFERENCE ON THE EUSTACHIAN TUBE AND MIDDLE EAR DISEASES

The Conference on the Eustachian Tube and Middle Ear Diseases will be held October 26-29, 1989, in Geneva. For further information, contact Prof Jacob Sade, Chairman, c/o The Secretariat, Conference on the Eustachian Tube and Middle Ear Diseases, Intercontinental Hotel Geneva, 7-9 CH du Petit Saconnex, CH-1211 Geneva 19, Switzerland.

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THICKNESS OF THE LATERAL SURFACE OF THE TEMPORAL BONE IN CHILDREN

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The placement of implantable auditory prostheses in children has raised questions concerning the thickness of the temporal bone in the region of implantation. The purpose of this study is to describe the thickness at specific sites of the lateral surface of the temporal bone in children of different ages. One hundred twenty-five intact temporal bones from 83 children of known sex, race, and age between birth and 20 years were measured. Thickness was measured with a specially designed micrometer at specific locations from a fixed reference point by use of a surface projected grid for site identification. Thickness was plotted against age on scattergraphs for each site, and regression analysis revealed a bimodal linear relationship. Sites medial to the temporalis muscle were the thinnest; sites associated with the posteroinferior insertion of the temporalis muscle, along the supramastoid crest, were the thickest. However, wide interindividual variability was the rule.

KEY WORDS — child development, growth, temporal bone.

A recent technologic advance in the fields of audiology and otolaryngology has been the development of the implantable bone conduction hearing device (Xomed Audiant Bone Conductor), an electromagnetic device that stimulates the cochlea directly via bone conduction from a magnet implanted in the temporal bone.

Adults and older children have undergone successful surgical implantation of the Xomed Audiant Bone Conductor, and use in younger children is progressing. This has raised questions regarding the thickness of the developing temporal bone.

The purpose of this paper is to report the lateral surface thickness of temporal bones obtained in children from birth to 20 years of age.

MATERIALS AND METHODS

One hundred twenty-five intact temporal bones from 83 individuals of known age, sex, and race were studied. The temporal bones used in this study were obtained from the skeletal collections located at three different institutions: 1) the Hrdlicka Collection and Terry Collection, both located at the Smithsonian Institute's Museum of Natural History in Washington, DC; 2) the Medical Museum of Walter Reed Hospital at the Armed Forces Institute of Pathology, Washington, DC; and 3) the Hammon Todd Collection and John Hopkins Fetal Skull Collection, both located at the Cleveland Museum of Natural History. The skulls and temporal bones examined from these collections were those of American children collected during the early 20th century and donated to the respective museums (Table 1).

All intact temporal bones accessible for thickness measurement and of documented sex, race, and age between birth and 20 years were included in the study group. If the temporal bone was damaged, in poor condition, or in an intact skull, making thickness measurement impossible, it was discarded. There was no preference given to age, sex, race, or cause of death in the collection of the data. If the right and left temporal bones of an individual were available, both bones were measured and treated as separate specimens.

The temporal bones studied were found either disarticulated from the remaining cranial bones, or intact, with a portion of the remaining cranial skeleton. The disarticulated bones were found most often among infants and children in whom death had occurred prior to maturation of the cranial sutures. In most of the older children, however, the temporal bones remained intact with the cranial skeleton. Most of the skulls were cut in a sagittal or circular manner at the time of autopsy. A sagittal cut through the sagittal suture and midline of the face did not interfere with the continuity of the

TABLE 1. NUMBER OF INDIVIDUALS AND TEMPORAL BONES MEASURED FROM EACH INSTITUTION

	No. of Individuals	*No. of Temporal Bones*
Smithsonian Institute Museum of Natural History	26	52
Armed Forces Medical Museum (Walter Reed)	2	3
Cleveland Museum of Natural History	55	70
Total	83	125

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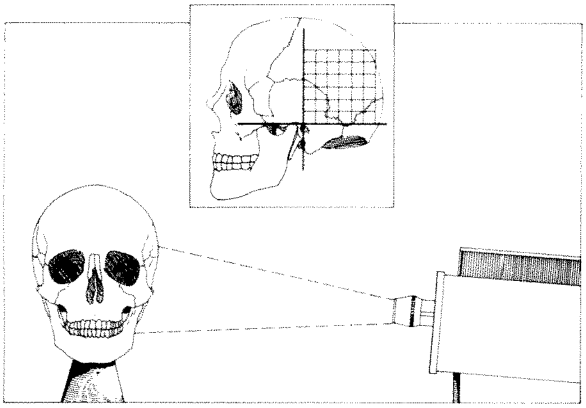

Fig 1. Each individual temporal bone or skull was positioned on stand, and template was projected onto lateral surface of bone from 35-mm slide projector. Axes of template were aligned such that each temporal bone, regardless of age, was measured in standardized fashion from predetermined reference point, ie, porion.

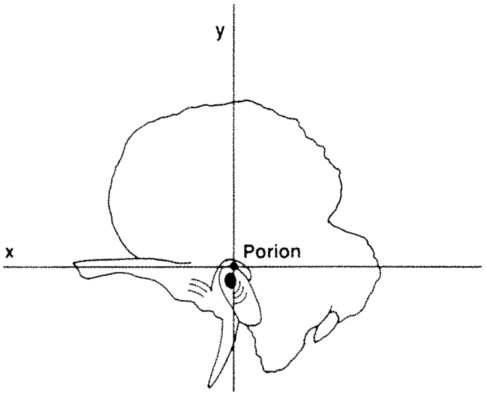

Fig 2. Horizontal and vertical template axes were positioned such that horizontal axis (x) bisected anteriormost portion of zygomatic arch and was tangent to superior and lateralmost aspect of bony external auditory canal. Central intercept of vertical and horizontal lines corresponded to most superior lateral point on roof of bony external auditory canal. This point is central point of reference in this study and is termed porion.

temporal bone, nor with the measuring process. However, circular cuts occasionally were made low enough to involve the temporal bone; if the temporal bone was damaged or altered in any manner, it was not considered in the study.

Each temporal bone and skull selected for measurement was secured on a stand specifically designed to hold the specimen stable and upright during the measuring procedure. By use of a standard 35-mm slide projector, a horizontal (x axis) and vertical (y axis) template with a grid was projected upon the lateral surface of the temporal bone (Fig 1). The horizontal axis was placed over the body of the zygomatic arch, bisecting the anterior end of the arch and tangent to the superior and lateralmost aspect of the bony external auditory canal. The central intercept of the vertical and horizontal axes was positioned to correspond to the most lateral superior point on the roof of the bony external auditory meatus. This was the central point of reference and was termed the porion (Fig 2). (The porion is a cephalometric landmark defined as the midpoint of the upper edge of the external auditory canal.[1]) The grid, a series of six parallel intersecting horizontal and vertical lines, was located within the posterosuperior quadrant. The projector was positioned at a distance away from the bone such that the interval between each of the projected lines forming the grid was exactly 1 cm (Fig 3). Only intersecting points on the lateral planar surface of the temporal bone were used as measurement points. Measurements were not taken at sites directly overlying the body of the petrous portion of the temporal bone (sites 1 and 2), sites thinned by broad suture lines superiorly, or sites posteriorly angled acutely away from the projected grid.

A specifically designed outside-measuring micrometer was constructed for use in measuring the thickness of the bone. The ends of the micrometer were fitted with ball bearing tips to aid conformation to the surface of the bone; the handle was equipped with a spring-loaded, geared ratchet stop to provide an equal and minimal measuring force at each point of measure. Each grid intersect point on the temporal bone was placed between the anvil end and the spindle end of the micrometer, and thickness measurements to one hundredth of a millimeter were obtained and recorded.

Each individual measurement, with age, sex, and race of the subject, was recorded and analyzed. The individual site measurements versus age were scattergraphed, and piecewise regression analysis was performed. Predictions for average thickness and percent of maximum thickness at selected ages then

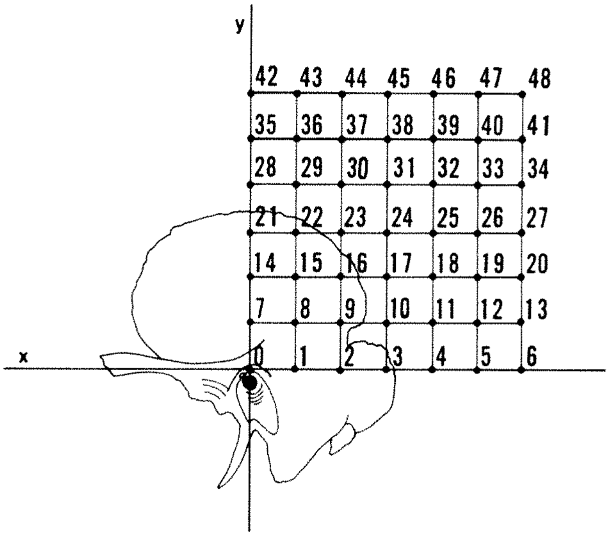

Fig 3. Posterosuperior quadrant was divided by six parallel intersecting horizontal and vertical lines, which provided 48 points of intersection. Projector was positioned at distance such that each line was 1 cm apart. Points of intersection then were numbered as shown.

TABLE 2. STUDY POPULATION DIVIDED ACCORDING TO RACE AND SEX

	White	*Nonwhite*	*Total*
Male	18	20	38
Female	19	26	45
Total	37	46	83

were calculated from the regression lines. The maximum thickness (100%) at each site was taken as the mean measurement value from those temporal bones at 20 years of age.

RESULTS

The temporal bones were those of 38 boys and 45 girls. The male group consisted of 47% whites and 53% nonwhites; the female group consisted of 42% whites and 58% nonwhites. A χ^2 value of 0.797 ($p = .372$) of the 2 x 2 contingency table (Table 2) showed that age and sex were independent variables within this study population and that random variation could account for the differences in subject numbers within groups of sex and race.

A frequency distribution chart for the number of measurements recorded per site is shown in Table 3. Site 7, which corresponds to a point located 1 cm superior to the porion, was the most frequently measured site and appeared on the surface of all bones studied. Site 8 was the second most frequently appearing site. As lateral expansile growth[2] of the temporal bone proceeded with increasing age, the number of sites measured per bone increased correspondingly.

The thickness measurements from each individual site, plotted as a function of age in years, and piecewise linear regression analysis suggested a bimodal linear relationship between thickness and age. There was a rapid early increase in thickness of the temporal bone during the first year of life, followed by a slower, sustained increase in thickness thereafter (Fig 4). The slope values for the group 0 to 1 year of age showed a tenfold increase in comparison to the slope values for the group 1 to 20 years of age. Despite the calculable linear progression, tremendous variations in thickness within each age were seen.

By rewriting the regression equation as thickness (mm) = (intercept) + (slope) x (age in years), the predicted average thickness and the percent of maximum thickness complete at various ages were calculated. The predictions for site average thickness and the percent of maximum thickness complete at selected ages are shown in Table 4.

By 10 years of age, all sites had estimates greater than 2 mm; the thinnest was site 14, with a value of 2.194 mm, and the thickest was site 9, with an estimate of 5.264 mm. At 20 years of age, all site estimates approached 3 mm; some were significantly thicker. Values for sites 3, 8, and 9 were at least 4 mm, representing the thickest areas of bone. Site 9 roughly corresponded to the course of the posteroinferior edge of the temporalis muscle insertion as it migrates in a posterosuperior direction over the surface of the temporal bone. Site 3 would often overlay the sigmoid sinus. The thinnest sites were generally those medial to the temporalis muscle, represented by sites 7, 14, 15, 16, 21, and 22, all of which had estimates below 4 mm.

TABLE 3. NUMBER OF MEASUREMENTS PER SITE FOR TWO AGE GROUPS

Site	*0-1 yr*	*1-20 yr*	*Total*
3	0	25	25
7	86	39	125
8	70	39	109
9	47	36	83
14	36	39	75
15	17	39	56
16	0	33	33
21	2	37	39
22	2	33	35

DISCUSSION

Cranial bones grow in response to tension produced by surrounding soft tissues, such as muscles and the expanding brain; the growth occurs on periosteal surfaces. Two periosteal surfaces are present: the outer table (cutaneous) and the inner table (meningeal). Each cortical table, or lamina, has a corresponding medullary, endosteal surface that is continuous with the trabeculae of the diploë.[3,4]

The cutaneous and meningeal periosteal sides of the cranial vault are entirely depository in nature; however, the endosteal surfaces of the laminae are resorptive in nature. The formation of bone on the periosteal surfaces and the resorption from the endosteal surfaces result in a net increase in thickness of the entire bony wall from expansion of the diploë and thickening of each individual plate. The outward movement of the cortical laminae of the cranial bones is produced by centrifugal displacement secondary to brain enlargement and is accompanied by formation of new bone at the suture lines; the intervening bone is somewhat quiescent during this movement, except for adjustments in proportionate thickness and curvature.

Todd[5] examined the skulls of 448 white men 20 to 80 years of age and reported that cranial thickness is quite variable and increases slightly with age up to approximately 50 years. Roche[6] measured cranial thickness on radiographs of white American children 3 months to 21 years of age. The average cranial thickness of boys exceeded that of girls at most points of measurement. He found a slightly bimodal growth rate, with more rapid growth below 5 years of age. We found the bimodal growth pattern to differentiate at about 1 year of age. An analysis of covariance performed on our data showed no significant thickness differences between sexes.

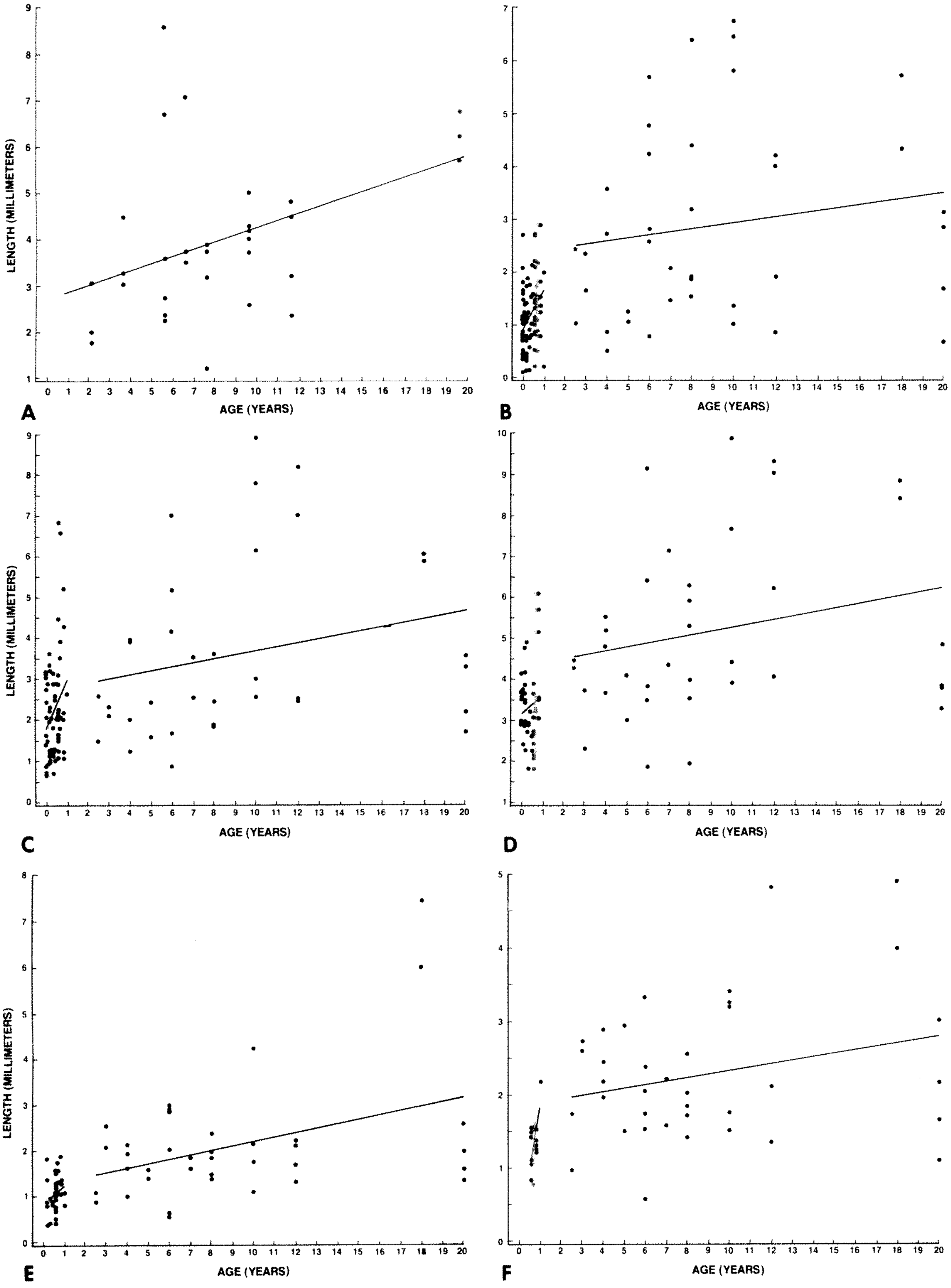

Fig 4. Thicknesses (length in millimeters) at specific sites were plotted as function of age; and piecewise linear regression analyses, shown as straight lines, were performed on data with a cutoff point of 1 year of age. A) Site 3. B) Site 7. C) Site 8. D) Site 9. E) Site 14. F) Site 15. (Continued on next page.)

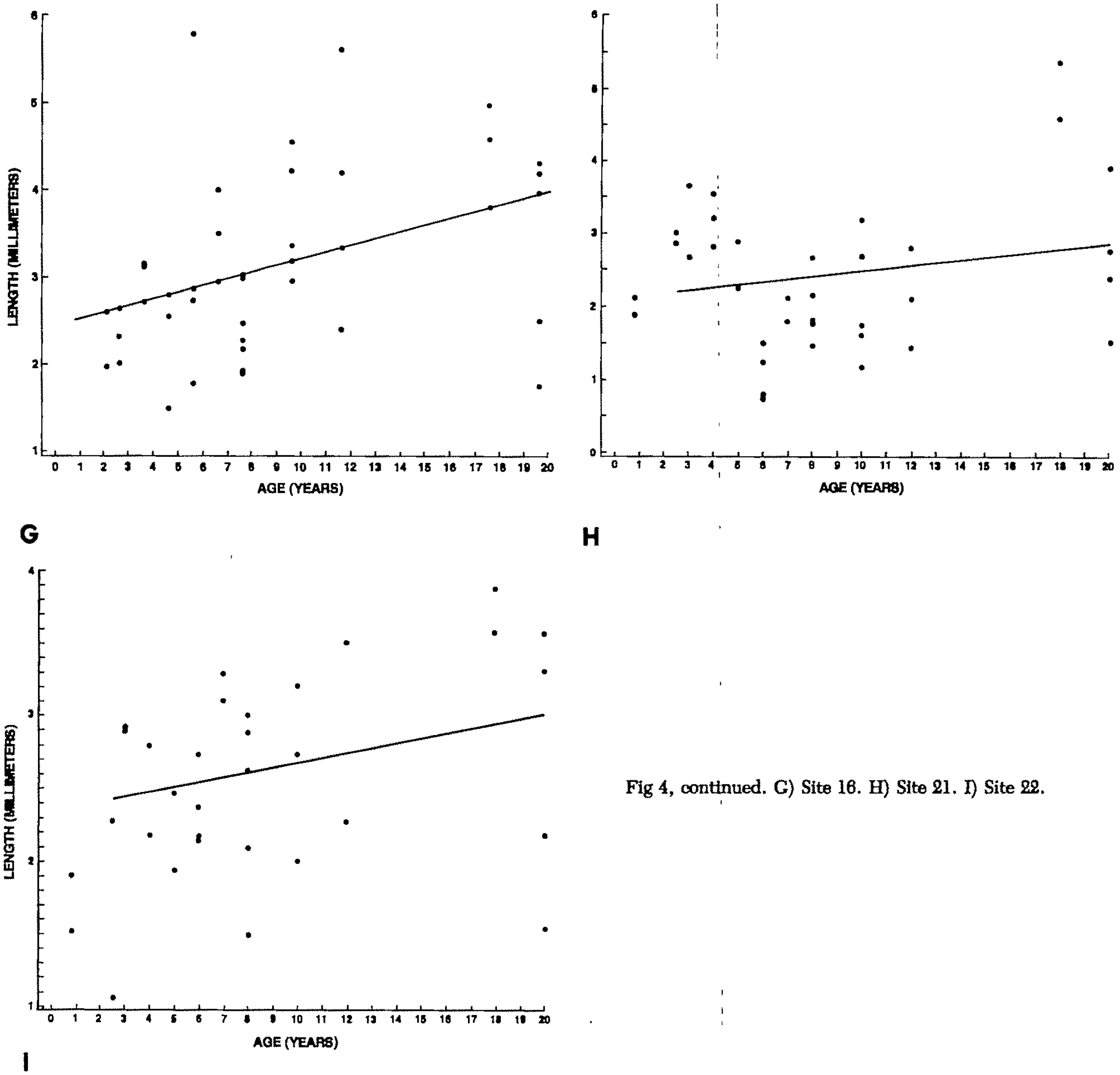

Fig 4, continued. G) Site 16. H) Site 21. I) Site 22.

Continued growth of skull thickness seems to occur slowly throughout adulthood. The skull seems to participate in age-related remodeling in a fashion unlike that in other parts of the skeleton, secondary to its structure of inner and outer cortical layers separated by cancellous bone.[7-11] Our study was confined to children, with an arbitrary cutoff point of 20 years.

In this study, the thickness of the temporal bone varied significantly from individual to individual within age groups; however, a number of general trends were observed.

The overall thickness of the temporal bone increased from anterior to posterior from site 7 to site 9 and from site 14 to site 16. Site 9, 2 cm posterior and 1 cm superior to the porion, was found to be the site of greatest thickness, regardless of age; the average thickness of this site was greater than 3 mm by 6 months of age and greater than 4 mm by 3 years of age. In only three children 3 years or older was this site less than 3 mm; the ages were 3, 6, and 8 years. There were some children, even to 20 years, in whom this site was greater than 3 mm but less than 4 mm; however, very few children 10 years or older had thicknesses less than 4 mm.

In summary, sites medial to the body of the temporalis muscle are the thinnest, and those sites that are associated with the posteroinferior insertion of the temporalis muscle, along the supramastoid crest, are the thickest; this is consistent with surgical observations.[12] However, it is imperative to recognize that there is wide variability in thickness regardless of age or site.

TABLE 4. PREDICTIONS FOR AVERAGE THICKNESS AND PERCENT MAXIMUM GROWTH BY AGE

Site		*Birth*	*6 mo*	*1 yr*	*3 yr*	*5 yr*	*10 yr*	*20 yr*
3	Ave (mm)				3.122	3.424	4.179	5.69
	% Max				54.8	60.2	73.4	100
7	Ave (mm)	0.895	1.264	1.634	2.519	2.633	2.918	3.487
	% Max	25.7	36.3	46.8	72.2	75.5	83.7	100
8	Ave (mm)	1.765	2.369	2.972	3.001	3.197	3.684	4.659
	% Max	37.9	50.9	63.8	65.0	68.6	79.0	100
9	Ave (mm)		3.369	3.584	4.605	4.793	5.264	6.205
	% Max		54.3	57.7	74.2	77.2	84.8	100
14	Ave (mm)		1.039	1.230	1.520	1.712	2.194	3.156
	% Max		32.9	38.0	48.2	54.2	69.5	100
15	Ave (mm)			1.820	1.996	2.089	2.231	2.786
	% Max			65.3	71.6	74.9	83.7	100
16	Ave (mm)				2.637	2.793	3.184	3.965
	% Max				66.5	70.4	80.3	100
21	Ave (mm)				2.225	2.298	2.484	2.854
	% Max				77.9	80.5	87.0	100
22	Ave (mm)				2.444	2.509	2.672	2.999
	% Max				81.5	83.7	89.1	100

Data are calculated from regression lines for each site at respective ages.

Ave — average thickness, % Max — percent of maximum growth.

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THE INTERNATIONAL SYMPOSIUM ON CLINICAL AND BASIC OTOLOGY

The International Symposium on Clinical and Basic Otology will be held June 4-6, 1990, in Beijing, People's Republic of China. The abstract deadline is December 31, 1989. For further information, contact the Beijing Institute of Otorhinolaryngology, Chan Liu, MD, Professor and Director, 17 Hougou Lane, Beijing 1000005, People's Republic of China.

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NERVE FIBER ANALYSIS OF THE FACIAL NERVE

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Nerve fiber analyses were conducted on the human facial nerve with use of a new staining method (Luxol-PAS-hematoxylin stain; discriminative staining method) that permits simultaneous observation of the axon and surrounding myelin sheath. The following combination of equipment was employed in the study: an image-analyzing digitizer, a microscope with a drawing tube, and a computer for storing the data and performing statistical analyses. The numbers, transverse areas, and circularity ratios of axons were measured in 11 cases. The average number of axons composing one facial nerve was 6,254, and the average size of the axons was 6.23 μm^2. The results indicated that although the numbers of axons became reduced with age, the transverse areas and circularity ratios of the axons did not change with age.

KEY WORDS — axon, facial nerve, Luxol fast blue–PAS-hematoxylin stain, morphometry, nerve fiber analysis, seventh cranial nerve.

INTRODUCTION

There are two main methods of nerve fiber analysis. One involves observation of the arrangement of the nerve fibers, and the other involves quantitative assessments by counting the nerve fibers and/or measuring them. The arrangement of the human facial nerve has been investigated by several authors,[1-6] and the pathway from the cisternal level to the stylomastoid foramen was confirmed by Hofmann[1] and by White and Verma.[2] As the next step, the facial nerve fiber arrangements in the facial nerve duct were examined by several researchers.[1,3-6] Quantitative studies on nerve fibers in the human facial nerve revealed a wide divergence among the total numbers given by different researchers.[7-11] The numbers of facial nerve fibers in the aging process were discussed only by Kullman et al.[10] The internal caliber of the myelin sheath was measured as the size of the nerve fibers.[7,8,10,11]

The aims of the present study were to elucidate the changes in the facial nerve fibers with age, to determine the size of the facial nerve fibers by measuring the transverse area of the axon, and to evaluate the deformity of axons based on their circularity ratios. This report thus provides a first step toward analyzing the changes of the facial nerve due to aging.

MATERIALS AND METHODS

Human facial nerve trunks with intermediate nerves and vestibulocochlear nerves were cut near the brain stem. The materials were taken from cadavers for anatomic dissection. The causes of death had no direct or indirect connection with the facial nerve. Two samples each were collected from the bodies of individuals who died in their 50s, 60s, 70s, and 80s, and one sample each was collected from the bodies of individuals who died in their 20s, 40s, and 90s.

After fixation of the nerves in 10% formalin, they were immersed in a secondary fixative composed of 5% potassium dichromate and 5% potassium chromate (1:4 in volume) with several changes for 3 weeks at room temperature. The blocks were embedded in celloidin after washing in running water and dehydration with alcohol. The celloidin blocks were sectioned transversely into 10- or 20-μm thick slices for staining with Luxol fast blue–PAS-hematoxylin, as devised by one of the authors (N.G.).[12] The sections were dehydrated and mounted in balsam. The shrinkage of the sections during their preparation amounted to approximately 10% in length.

For measurement and analysis of the facial nerve, a combination of a microscope, drawing tube (or camera lucida), electronic optical planimeter (Digiplan, Kontron Co), and computer (PC-9801VX2, NEC) was adopted. Enlarged images (50 times) of transverse sections of the facial nerves were used to measure the transverse areas of the nerves without surrounding or intervening connective tissues, and more enlarged images (536 times) were used to measure the transverse areas of the axons and to count the numbers of axons with a diode piloting tracer. For the measurement of the nerve fibers, five sites of systemic sampling were selected as shown in Fig 1. Each sampling area consisted of a 0.14 x 0.14-mm square.

RESULTS

Numbers of Nerve Fibers. The numbers of facial nerve fibers were 4,486 to 7,570 (average, 6,254). All data are listed in the Table. Most fibers were myelinated (each with a blue-green myelin sheath

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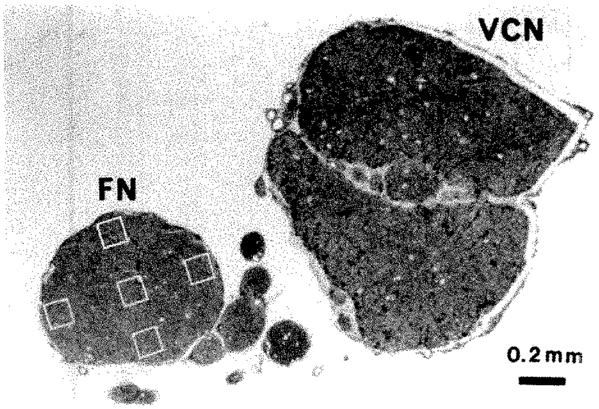

Fig 1. Transverse section of facial nerve (FN) and vestibulocochlear nerve (VCN). Five squares on FN indicate sites of systematic sampling.

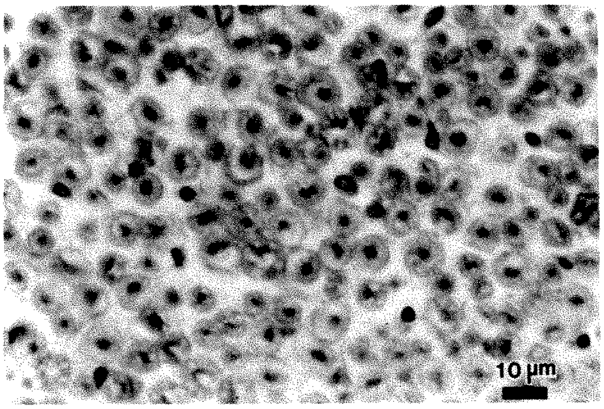

Fig 2. High-power view of facial nerve (Luxol-PAS-hematoxylin stain).

surrounding a dark purple or black axon; Fig 2), and only a few were unmyelinated. There were no differences in numbers of fibers among the five sites. The numbers of nerve fibers showed a slight decrease with age, except for one subject (subject 10, an 85-year-old man).

Size of Nerve Fibers and Axons. The size of the nerve fibers (area of transverse sections of the facial nerve without connective tissue) was between 0.275 mm^2 and 0.725 mm^2 (average, 0.424 mm^2). The data are listed in the Table. The sizes of the axons (areas of the axons in transverse section) ranged from 4.79 μm^2 to 8.58 μm^2 (average, 6.23 μm^2) (see Table). There was no clear difference of size among the five sites in each subject. The distribution of the transverse areas of the axons is illustrated in Fig 3. The transverse areas of the axons in each case revealed a normal distribution (standard deviation, 2.5 to 4.0). Samples from the bodies of individuals who died in their 60s, however, showed a slightly wide distribution. The sum of the transverse areas of the axons in each subject ranged from 0.0273 mm^2 to 0.0511 mm^2 (average, 0.0385 mm^2), or 6.1% to 14.8% (average, 9.5%) of the total area of the transverse sections of the facial nerves.

Circularity Ratio. The circularity ratio (CR) of the transverse sections of the axons was calculated as follows:

$$CR = 4\pi \text{area(in mm}^2\text{)}/(\text{perimeter[in mm]})^2$$

The CR in each subject is listed in the Table. The distributions are shown in Fig 3. The average CRs of each decade ranged from 0.67 to 0.89 (average, 0.79). The peak of the distribution of the CRs was between 0.8 and 0.9 in every subject. Circles and ovals of which the CRs were 1.0, 0.8, and 0.6 are shown in Fig 4. Axons in which the CRs were lower than 0.6 represented from 4% to 39% (average, 16%) of the total axons. Individuals who died in their 60s had a few low-CR axons, but those who died in their 70s had many of them. The CRs were thus higher in the seventh decade than in the eighth decade.

DISCUSSION

There are several reports on the numbers of human facial (motor) nerve fibers.[7-11] According to these reports, the total numbers of facial nerve fibers on one side ranged from 4,465 to 20,307 at the posterior cranial fossa or facial canal part. Our data (from 4,486 to 7,570; average, 6,254) were within the above range, and also in accordance

RESULTS OF FIBER ANALYSES OF FACIAL NERVES

Subject	*Age*	*Sex*	*No. of Facial Nerve Fibers*	*Average Area of Facial Nerve (mm^2)**	*Average Area of Axon (μm^2)†*	*Sum of Areas of Axons (mm^2)†*	*Area Ratio of Axons to Nerve Fibers*	*Circularity Ratio (See Text)*	*% of Circularity Ratios < 0.6*
1	24	M	6,932	0.725	7.37	0.0511	0.070	0.87	10
2	43	M	7,155	0.414	5.12	0.0366	0.088	0.67	13
3	54	M	7,570	0.401	5.59	0.0423	0.105	0.82	17
4	57	M	7,192	0.448	6.08	0.0437	0.098	0.83	12
5	66	F	5,197	0.367	8.58	0.0443	0.121	0.89	4
6	69	F	5,274	0.275	7.65	0.0403	0.147	0.85	7
7	74	F	6,441	0.504	4.79	0.0309	0.061	0.67	39
8	76	M	6,191	0.431	5.37	0.0328	0.076	0.70	29
9	85	F	5,303	0.347	5.82	0.0309	0.089	0.76	21
10	85	M	7,057	0.473	6.10	0.0430	0.091	0.82	14
11	92	F	4,486	0.284	6.08	0.0273	0.096	0.82	14
Average			6,254	0.424	6.23	0.0385	0.095	0.79	16

*In transverse sections without connective tissue.

†In transverse sections.

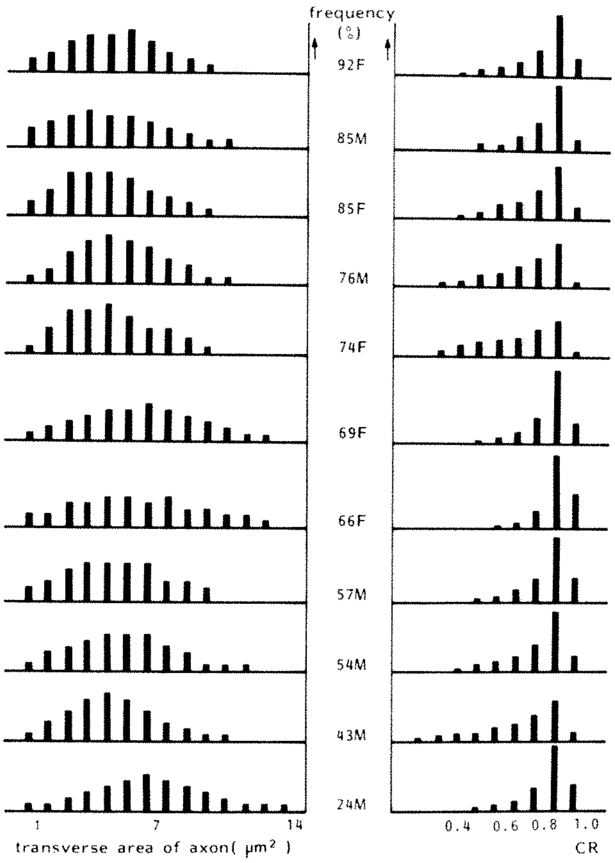

Fig 3. Distributions of axonal areas and circularity ratios (CRs). Age and sex of subjects are given in center column.

with the estimated number of cells in the facial nerve nucleus of 4,500 to 9,460.[8] In his report, van Buskirk[8] dealt with 28 subjects but did not identify their ages. Kullman et al[10] dealt with ten subjects whose ages ranged from 9 weeks to 89 years. The other authors' reports concerned relatively few subjects. We examined 11 subjects whose ages covered almost all decades. The data revealed a slight decrease in numbers of facial nerve fibers with age (Fig 5). A scatter diagram and regression line between the numbers of nerve fibers and ages are shown in Fig 5. None of the previous reports indicated any decrease in the numbers of facial nerve fibers with age.

The size of the nerve fibers of the facial motor nerve was determined previously from the internal caliber of the myelin sheath.[7-11] The average diameters given in the references were 7 to 9,[7] 7 to 10,[8] 6 to 8,[9] 3 to 7,[10] and 7 to 9 μm.[11] Myelinated nerve fibers of the vestibulocochlear nerve also were measured by the same method.[13-15] Kullman et al[10] determined the internal calibers of myelin sheaths and presented histograms of the myelinated fiber sizes of facial nerves in ten subjects of various ages. They reported that the histograms of the facial nerves did not show a consistent pattern at the mastoid portion. Apart from this, there are no other reports in the literature that analyze facial nerve fibers during the process of aging. Their study therefore has been considered important for the nerve fiber analysis of the facial nerve. However, it is not guaranteed that the internal caliber and shape of the myelin sheath actually represent the diameter and shape of the axon. Concerning the transverse areas of nerve fibers, there are measurements with values (30 to 80 μm^2)[7-11] that are much larger than ours (5 to 9 μm^2). The reason for this large disparity may be that they measured the internal caliber of the myelin sheath (the data were calculated by us as a circle from the given caliber), while we measured the axonal area itself as the nerve fiber size. We sometimes observed a very thin gap between the axon and the myelin sheath in many nerve fibers. Although this gap could be due to an artifact caused by the methods used, we have no data regarding this possibility.

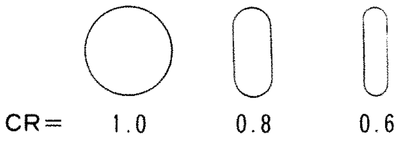

Fig 4. Circularity ratios (CRs) and probable shapes of axons.

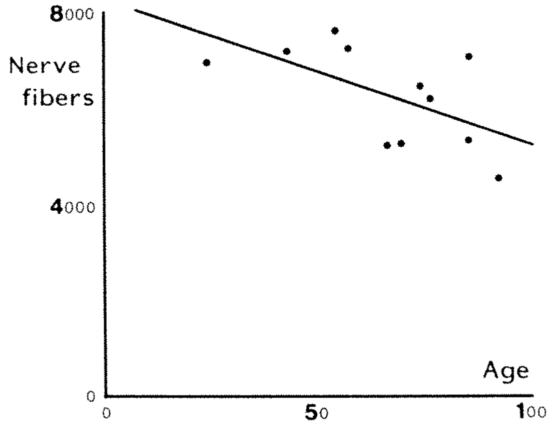

Fig 5. Scatter diagram and regression line between numbers of nerve fibers and age ($r = -0.59$).

There are relatively few reports available on nerve fiber analysis. The reasons may be that the caliber of the myelin sheath was measured instead of the axon itself, since it was impossible previously to stain the axon and myelin sheath discriminatively for light microscopic observation, and that the development of electron microscopic procedures that were suitable for the observation of nerve fibers[2,5,16] did not contribute much to quantitative nerve fiber analysis.

Our research had several unique characteristics: 1) we directly measured the axonal areas of transverse sections of the facial nerve after confirming the presence of axons and surrounding myelin sheaths; 2) the new staining method (Luxol-PAS-hematoxylin stain; discriminative staining method) adopted for the study permitted every structure (axon, myelin sheath, nucleus, nucleolus, Nissl's bodies, connective tissue, amyloid bodies, lipofuscin granules, vessels, etc) to be recognized easily; and 3) the combination of an image-analyzing digitizer, a microscope with a drawing tube, and a computer for storing the data and performing statistical analyses made this kind of research both accurate and easy. It was extremely difficult or impossible before the introduction of the image analyzer to measure the areas of irregular shapes accurately.

The authors constructed histograms of the axonal area distributions in all subjects. These showed normal distributions among almost all decades (Fig 3). The data suggested that the aging process of the facial nerve produced no decrease connected with particular sizes of nerve fibers. Kullman et al[10] reported that histograms of the myelinated fiber sizes of facial nerves at various ages did not show a consistent pattern. The reason they did not exhibit normal distributions may be that the histograms contained components of the facial (motor) nerve fibers and chorda tympani nerve fibers. In order to measure and count the nerve fibers in the present study, only one transverse section in every decade was used to trace the margin of the axon with a piloting tracer, confirming the presence of axons and surrounding myelin sheaths. There is no previous report dealing with interrelated measurements of the size (area), perimeter, and number of nerve fibers in sections.

The shapes of axons cut tangentially (or transversely) are not always found to be circular or oval. They are sometimes club-shaped, crescent-shaped, asterisk-shaped, or irregular. Circularity ratios therefore were introduced in order to evaluate these deformities from a morphologic point of view. Circular or oval axons have CRs of over 0.6, reaching a peak of between 0.9 and 0.8 (Figs 3 and 4). On the other hand, CRs below 0.6 indicate that the axons may be club-shaped, crescent-shaped, asterisk-shaped, or irregular. In the present study, we found no relation between aging and the percentages of nerve fibers with CR values below 0.6. Analyses of the shapes and morphometry of the axons such as of their CRs have not been given in the literature.[7-11,17]

It is important to collect accurate data on the normal nerve fibers of subjects of different ages before undertaking an analysis of the nerve fibers of subjects afflicted by neurologic diseases. Some researchers[18,19] have reported changes in the sizes of the facial nerve with development and aging. However, there is no previous report presenting a nerve fiber analysis of the facial nerves of subjects of different ages, apart from the data of Kullman et al.[10] Their study concerned only ten subjects in all, while our data cover only one or two subjects in each decade. It seems reasonable to conclude that the number of facial nerve fibers decreases slightly with age, but there is no evidence that the axonal area or the CR of the axons decreases with age. It is desirable that many more samples be examined in order that these tentative conclusions can be confirmed and that a detailed analysis can be undertaken.

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HYALURONAN IN EXPERIMENTAL SEROUS AND PURULENT OTITIS MEDIA

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The concentration of hyaluronan (hyaluronic acid; sodium hyaluronate; HA), a major component of connective tissue, was analyzed by a specific radioassay in tissue samples from normal rat middle ears and in tissue and effusions from middle ears affected by experimentally induced otitis media. In normal ears the pars flaccida of the tympanic membrane contained a considerably higher concentration of HA (60 to 200 μg/g) than the pars tensa and areas of the medial wall (2 to 7 μg/g). In purulent otitis media the pars flaccida contained less HA than in normal ears. The HA concentrations were lower in purulent (3 to 40 μg/mL) than in serous (20 to 190 μg/mL) effusions. The weight average molecular weight of HA in serous fluid was high ($> 10^6$) and comparable to that in lymph. It is inferred from the study that the subepithelial tissue and its matrix components, eg, HA, must be considered when attempting to understand the function of the middle ear normally and in otitis media.

KEY WORDS — connective tissue, hyaluronic acid, inflammation, middle ear, otitis media, rat, tympanic membrane.

INTRODUCTION

In recent years, increasing importance has been attached to the subepithelial connective tissue layer in middle ear physiology and pathophysiology. This layer seems to undergo dynamic morphologic changes when affected by the various forms of otitis media.[1] In inflamed middle ears the connective tissue cells increase in number and are considered to be intimately involved in the inflammatory and immunologic reactions, which may be responsible for the pathogenesis of middle ear effusions.[2]

Animal models can be used to assess the sequential changes taking place in the middle ear cavity when various forms of experimental otitis media are induced.[3] In the rat, well-defined types of serous and purulent otitis media (SOM and POM) can be induced by blocking the eustachian tube or by splitting the soft palate.[4,5]

Hyaluronan (hyaluronic acid; sodium hyaluronate; HA)[6] is an element ubiquitously distributed in the extracellular matrix. Recently we[7] reported that HA occurred in mucoid middle ear effusion material of patients with SOM at levels that were high compared with those found in serum. Hyaluronan was considered to be a sign of connective tissue involvement. It could possibly play a role in modulating the inflammatory process.

In the present study the concentration of HA was determined in tissue samples from well-defined areas of normal rat middle ears and of middle ears affected by SOM and POM. The concentration of HA in the effusion materials was analyzed after various intervals following the induction of the inflammatory conditions. Furthermore, the molecular weight distribution of HA was determined in serous effusion material.

MATERIAL AND METHODS

Healthy adult male Sprague-Dawley rats weighing 250 to 350 g were used for the study. They were anesthetized by injecting methohexital sodium (Brietal) into a tail vein and then subjecting them to the following experimental procedures.

Normal Middle Ears. In 25 untreated rats, tissue pieces were resected from four well-defined areas of the middle ear, as shown in the Figure (pars tensa and pars flaccida of the tympanic membrane, the mucosa of the nasal fossa, and the occipital sulcus of the medial wall[8]), pooled in groups of five in preweighed sealed cups, and weighed. The pooled tissue samples were frozen within 1 hour of sampling and stored at −20°C until the HA concentration was analyzed.

Serous Otitis Media. In 31 rats the left tympanic bulla was dissected free under aseptic conditions through a midline approach. A small hole was drilled in the bottom of the bulla by use of a scalpel and a gutta-percha plug (De Trey, Switzerland) hermetically inserted into the tympanic orifice of the eustachian tube. After this operation the animals were kept under normal laboratory conditions until killed painlessly after the time periods shown

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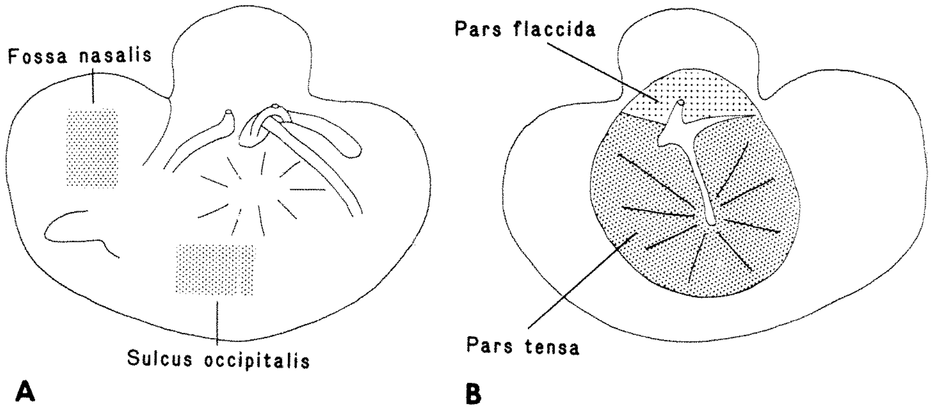

Sites of sampling in rat middle ear. A) Medial wall. Mucosal samples were taken from nasal fossa and occipital sulcus. B) Lateral wall. Tissue samples were taken from pars flaccida and pars tensa of tympanic membrane.

in Table 1. After decapitation the left middle ear was reopened through a hole in the bottom of the bulla. All of the serous effusion material was aspirated and the cavity carefully rinsed with 2 x 25 μL of 0.1 *M* phosphate buffer, pH 7.2. The aspirator also was rinsed with 2 x 25 μL of the same phosphate buffer, and the rinsing solutions were added to the aspirated serous effusion material. The fluid from one ear was diluted further with phosphate buffer to a final volume of 0.25 mL. As the rat middle ear has a volume of about 50 μL,[9] its contents were regarded as fivefold diluted. Samples then were taken for analysis of the HA concentration. In five of the rats with SOM, induced 28 days earlier, tissue samples were obtained from the left middle ear in the areas described in the Figure. The samples were pooled, weighed, and stored as described above for normal middle ears.

Purulent Otitis Media. In 14 rats the soft palate was split with a scalpel along the midline from the posterior free border to the hard palate. Afterwards the animals were kept under normal laboratory conditions until POM evolved bilaterally. The animals were killed painlessly by decapitation after the time periods shown in Table 2. Then the left and right middle ears both were opened through a hole in the tympanic bulla. All of the purulent effusion material was aspirated, collected, and prepared for the HA analysis as described for the ears with SOM.

TABLE 1. HYALURONAN CONCENTRATIONS AND MOLECULAR WEIGHT DISTRIBUTIONS IN MIDDLE EAR EFFUSIONS OF RATS WITH EXPERIMENTALLY INDUCED SOM

Days After Induction of SOM	*Hyaluronan Concentration in μg/mL*		*Weight Average Molecular Weight*	*Number Average Molecular Weight*
	Mean ± SEM	*Range*		
3	70.6 ± 9.6 (n = 6)	43.7- 95.0	ND	ND
6	86.0 ± 16.8 (n = 4)	53.7-129.3	3.6 x 10^6 (n = 3)	5.2 x 10^5 (n = 3)
9	75.4 ± 10.0 (n = 11)	20.0-120.3	ND	ND
14	83.9 ± 20.5 (n = 4)	26.2-116.5	ND	ND
28	94.8 ± 22.2 (n = 6)	25.3-190.0	1.3 x 10^6 (n = 6)	1.5 x 10^5 (n = 6)

SOM — serous otitis media, ND — not determined.

Pieces of tissue were obtained from the four areas described in the Figure from ten middle ears of five rats that had POM for 24 days, and from eight middle ears of four rats that had POM for 32 days. The tissue samples were handled as described for normal animals.

Determination of Hyaluronan Concentration. In tissue samples from normal ears and ears with POM, the HA concentration was determined by a radioassay based on the specific affinity of cartilage proteins for HA.[10] The method, which is similar to a radioimmunoassay, had been modified earlier for protease-treated tissue samples[11] and direct determinations of HA in serum.[12] In the present study the tissue samples were extracted with 200 μL buffer solution (0.05 *M* sodium acetate; 1.5 *M* sodium chloride, pH 5.8) for 16 hours at room temperature. Then 150 μL of the solution was withdrawn and used for HA determination. The tissue samples were further extracted with 200 μL 4 *M* guanidinium chloride in 0.5 *M* sodium acetate, pH 5.8 (an established solvent to dissociate HA-proteoglycan aggregates[13]) for 20 hours at room temperature. The HA concentration was determined as previously described,[11] except that the calibration standards were dissolved in solutions identical to those used for extracting the tissues.

The tissues from rats with SOM were handled as described above except that the extracts were desalted on a Sephadex G25 column before the HA concentration was determined.[11]

TABLE 2. HYALURONAN CONCENTRATIONS IN MIDDLE EAR EFFUSIONS OF RATS WITH EXPERIMENTALLY INDUCED POM

Days After Induction of POM	*Hyaluronan Concentrations in μg/mL in Left and Right Ears*		*Left Ears*	*Right Ears*
	Mean ± SEM	*Range*	*Mean*	*Mean*
9	18.8 ± 3.3 (n = 9)	8.0-42.2	22.3 (n = 5)	14.4 (n = 4)
24	18.4 ± 2.3 (n = 9)	3.0-29.8	18.4 (n = 4)	18.4 (n = 5)
32	9.8 ± 2.7 (n = 7)	2.4-21.8	10.2 (n = 4)	9.4 (n = 3)

POM — purulent otitis media.

TABLE 3. TISSUE CONCENTRATIONS OF HYALURONAN (μg/g) IN RATS WITH NORMAL MIDDLE EARS AND EARS WITH SOM AND POM

	Occipital Sulcus	*Nasal Fossa*	*Pars Tensa*	*Pars Flaccida*
Normal middle ears				
Pooled sample No. 1 (n = 5)	3.1	4.3	4.6	105.6
Pooled sample No. 2 (n = 5)	2.8	7.2	1.7	81.7
Pooled sample No. 3 (n = 5)	2.7	3.5	5.5	81.5
Pooled sample No. 4 (n = 5)	1.9	4.2	4.1	60.8
Pooled sample No. 5 (n = 5)	3.5	4.2	4.4	193.0
Middle ears with otitis media				
SOM 28 days* pooled sample (n = 5)	11.0	11.0	22.0	132.0
POM 24 days* pooled sample (n = 10)	6.0	8.4	29.3	32.1
POM 32 days* pooled sample (n = 8)	27.7	5.2	8.1	15.4

SOM — serous otitis media, POM — purulent otitis media.

*Time between induction of otitis media and painless killing.

The effusion material in SOM and POM was analyzed for its HA concentration with the specific radioassay.[11] However, before analysis of the purulent effusion material, the mucin was solubilized by reduction and alkylation as previously described.[7]

Determination of Molecular Weight Distribution of HA. Equal volumes of serous middle ear effusion material from three animals killed after 6 days and from six animals killed after 28 days were pooled as indicated in Table 1. The molecular weight distribution of HA in the pooled samples was determined by a gel chromatographic method,[14] and the weight and number average molecular weights were calculated.

RESULTS

Normal Middle Ears. The total HA content in pooled tissue samples from the four areas of the middle ear is shown in Table 3. Roughly equal amounts of HA were extracted with acetate buffer and guanidinium chloride. The pars flaccida of the tympanic membrane exhibited a considerably greater concentration of HA vis-à-vis the pars tensa and the two mucosal areas of the medial wall.

Serous Otitis Media. The concentration of HA in middle ear tissues from rats that had SOM for 28 days is shown in Table 3. The concentration in the pars flaccida did not differ from that found in normal ears, whereas the other tissue sites showed a slight increase in HA concentration compared with the controls.

The concentration and the molecular weight distribution of HA in the effusion material collected between 3 and 28 days after the induction of the inflammatory condition are shown in Table 1. The concentration remained at approximately the same high level irrespective of the duration of SOM. The molecular weight decreased slightly with time, but the weight average was still high $(>10^6)$.

Purulent Otitis Media. The concentrations of HA in middle ear tissues from rats that had POM for 24 and 32 days are shown in Table 3. The pars flaccida of the POM ears contained considerably less than the normal amount, whereas the other tissue sites showed variable but slightly increased HA concentrations.

The concentrations of HA in the purulent effusion material, collected at 9, 24, and 32 days after the induction of the otitis media (Table 2), were lower than in serous effusion material (Table 1). On comparing the right and left ears, the HA concentrations were in the same range.

DISCUSSION

Hyaluronan is a high molecular weight polysaccharide that is present in every tissue and tissue fluid. Its concentration, however, varies within a wide range, with the highest values found in loose connective tissue and the lowest in blood serum.[15] In tissues, HA occurs either as a coat attached to cell surfaces, aggregated with other macromolecules such as cartilage proteoglycans, or as a free glycosaminoglycan, eg, in synovial fluid and the vitreous humor of the eye.

Hitherto, no information has been available concerning the distribution of HA in middle ear structures, though HA and other glycosaminoglycans have been identified in human middle ear effusions.[7,16] We were able to show[7] that HA occurs in mucoid middle ear effusions of children at concentrations that were high compared with those of serum.

The present study has shown that HA occurs in middle ear tissues at all sites analyzed, but with regional differences. The concentration of HA is considerably higher (20- to 30-fold) in the pars flaccida of the tympanic membrane than in the pars tensa or the two well-defined mucosal areas on the medial wall. This is an interesting observation, as the pars flaccida is structurally different from the pars tensa, eg, in fiber composition, occurrence of mast cells, and innervation.[17-19]

The HA concentration of the middle ear tissues from rats with SOM is almost the same as that determined for normal animals, whereas in POM the pars flaccida contains a lower concentration of HA. It is noteworthy that in histologic sections the structure of the pars flaccida is less altered in SOM than in POM.[20] In POM the connective tissue layer of the pars flaccida is thickened and invaded by abundant inflammatory cells. It is conceivable that the low HA values in the pars flaccida in POM can be attributed at least partly to the action of invading inflammatory cells. Neutrophils and macrophages produce oxygen-derived free radicals that can degrade HA.[21] On the other hand, it is also possible that HA can be degraded by hyaluronidase and other enzymes that are present in bacterial middle ear effusions.[22] Bacteriologic cultures of purulent middle ear effusion material provoked by cleavage of the soft palate in rats have revealed an initial growth of gram-positive cocci that is later changed to a gram-negative flora (Johansson et al, unpublished observations).

The earliest samples of middle ear effusion material, after induction of SOM and POM, were collected when the middle ears were filled completely with fluid, at 3 and 9 days, respectively, when HA was already present. The concentration in the effusion of SOM was higher than in that of POM. In SOM the HA content remained at approximately the same level throughout the study, whereas in POM it had a tendency to decrease with time. Serous effusions provoked in the present manner are sterile (Johansson et al, unpublished observations), and thus bacterial degradation should be negligible. The HA remained in a high molecular form, and it is unlikely that the large HA molecules can be absorbed via the mucosa.[23] The study thus indicates a slow turnover of HA in the serous effusion. The concentrations of HA in both serous and purulent effusion materials in the present experimental models correspond relatively well to that in mucoid middle ear effusions from patients.[7]

Interestingly, the effusion materials collected from SOM ears in the present study were shown to contain HA in concentrations on the same order as those found in the pars flaccida. In recent studies the pars flaccida has been shown to take part in the production of effusion material in experimental otitis media.[24] It is tempting to suggest that HA in serous middle ear fluid may have leaked from the pars flaccida during the initial stage of the SOM.

The HA levels were lower in purulent than in serous effusion materials. As discussed for the tissue levels of HA in SOM and POM, this discrepancy may result from the degradation of HA by the action of inflammatory cells and/or bacteria.[21,22] The concentrations of HA in both serous and purulent effusions were 1,000-fold higher than in circulating blood and quite comparable to those determined for lymph.[25] Also, the molecular weight distribution of HA in pooled samples of serous effusions corresponds better to the distribution of HA from lymph than that from serum.[25] Paparella et al[26] have suggested that middle ear effusions originate through a passive transfer of serous fluid from the subepithelial vessels into the middle ear. However, they also demonstrated an increased amount of intercellular fluid consistent with a possible lymphostasis. There is also experimental evidence that obstruction of the lymphatic drainage from the middle ear and the eustachian tube can cause effusion in experimental otitis media.[27] The findings in the present study favor the latter proposition in that serous middle ear effusions contain a component, HA, originating from lymph rather than from serum.

The significance of the observation that HA is present in the middle ear is related to the important physiologic functions assigned to the molecule.[15] At high concentration in the extracellular matrix, HA offers considerable resistance to bulk flow of water. It also has a high osmotic buffer capacity, which significantly contributes to the water homeostasis in the body. It stabilizes the structure of the extracellular matrix through specific binding to the protein in proteoglycans. The HA network formed in the tissues may exclude macromolecules and may act as a filter for molecules that are diffusing through the matrix. Also, HA has specific cell-to-cell and cell-to-surface interactions, as well as various cell biologic effects. Several reports have been cited previously[15] on interactions between HA and macrophages, granulocytes, and lymphocytes, respectively. High concentrations of high molecular weight HA inhibit the cell movements and phagocytosis by granulocytes, while lower concentrations enhance phagocytosis and pinocytosis. Furthermore, HA could regulate various cellular activities involved in reparative processes, and recently a hypothesis for HA interacting with fibrin in the early phase of wound healing was discussed.[28]

The subepithelial connective tissue is neglected in most studies on the middle ear mucosa. However, recent studies have indicated that many important reactions occur in this structure during pathologic conditions.[1,2,20] The present study has shown that middle ear tissues exhibit significant amounts of HA. In inflammatory conditions of the middle ear, the effusion material contains comparatively high concentrations of this polysaccharide. It is postulated that HA in these effusions originates from the subepithelial connective tissue, with a significant contribution from lymph.

Our findings give further support to the view that the subepithelial tissue and its matrix components, eg, HA, must be considered when we attempt to understand the function of the middle ear under normal conditions and in various inflammatory disorders.

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OPTOKINETIC AFTERNYSTAGMUS IN HUMANS: NORMAL VALUES OF AMPLITUDE, TIME CONSTANT, AND ASYMMETRY

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It has been suggested that the appearance of directional asymmetry and/or a reduced time constant of optokinetic afternystagmus (OKAN) might be a clinical index of vestibular imbalance. However, we do not know the limits for OKAN parameters in normal humans. Accordingly, we studied OKAN in 30 normal subjects using a "sampling" method, in which a number of values of OKAN are obtained by turning out the lights periodically during optokinetic stimulation. We found that the initial velocity of OKAN has a large intrasubject variability. Accordingly, if precision is desired so as to obtain 95% confidence that the measured mean of the initial velocity of OKAN is within 25% of the true mean in an individual subject, at least eight measurements of the initial OKAN velocity must be taken. When 12 measurements are made, all subjects had a minimum value of 5°/s initial OKAN, and there was little directional asymmetry (mean of $-0.47°/s \pm 3.13°/s$). The intrasubject variability of the time constant of OKAN was similar to the variability of initial OKAN velocity. However, because it is not possible to obtain repeated measures of the time constant in a short period of time, the time constant of OKAN is less likely to be useful in clinical testing.

KEY WORDS — optokinetic afternystagmus.

INTRODUCTION

In normal humans, movement of the entire visual environment induces a compensatory rotation of the eyes called optokinetic nystagmus (OKN). Although OKN is evaluated routinely in patients with vestibular diseases, it is an insensitive test for detecting vestibular lesions.[1] This is not surprising, as OKN in humans is generated mainly by a visual tracking system (pursuit) that is relatively independent of the vestibular system.[2]

Zee et al[3] suggested that optokinetic afternystagmus (OKAN) might be a sensitive indicator of a vestibular lesion. If the lights are extinguished during OKN, eye movements continue for a period of 10 to 30 seconds, as OKAN, with a gradually declining slow-phase velocity. It is thought that OKAN reflects the component of the optokinetic response due to activation of the vestibular nucleus.[4]

Experimental and clinical studies have shown the importance of the vestibular system in the generation of OKAN. Bilateral labyrinthectomy completely abolishes OKAN both in animals[5-7] and in humans.[3] In monkeys, immediately after unilateral labyrinthectomy, OKAN is decreased in duration and asymmetric in gain.[5,7,8] Even after several months, monkeys still exhibit OKAN of less duration than normal.[5,8] Humans with unilateral vestibular lesions also may show similar asymmetric OKAN.[9,10] Accordingly, significant asymmetry of OKAN may be a sign of unilateral labyrinthine lesions, and loss of OKAN may indicate bilateral labyrinthine dysfunction.

Given that measuring OKAN in humans might be a method of detecting a vestibular lesion, an important practical question is, "What are the limits of the normal behavior to which values in patients are to be compared?" Three variables are commonly used to quantify OKAN. These are the initial slow-phase velocity, the time constant of decay, and the directional asymmetry of the responses to rightward and leftward stimulation. We studied OKAN to establish a range of normal values for these parameters, as well as to obtain a measure of intrasubject variability.

METHODS

Thirty normal subjects ranging in age from 22 to 81 years were studied. None had dizziness or other complaints referable to the vestibular system or had taken drugs known to affect eye movements. The subjects were divided into three groups by age, each consisting of five women and five men: group 1 included subjects 22 to 35 years of age (average, 27.1 years), group 2, 36 to 50 years of age (average, 40.7 years), and group 3, 51 to 81 years of age (average, 60.6 years).

The subjects were seated inside a 1.2-m diameter optokinetic drum. The inside of the drum had black squares placed randomly on a white background and extended 1 m above and below the line of

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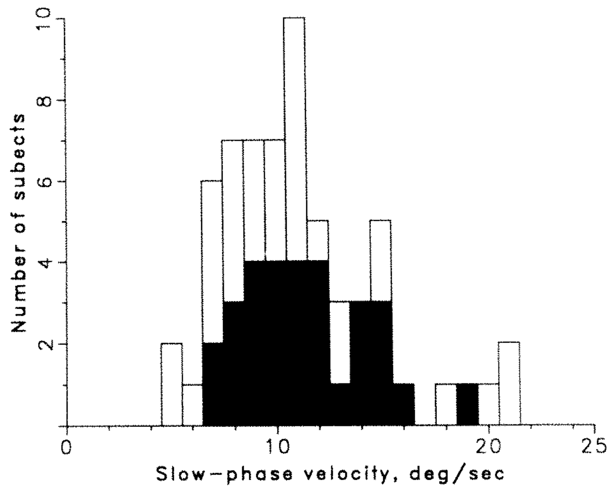

Fig 1. Histogram of distribution of optokinetic afternystagmus initial velocity based on sample values. For each subject, mean values of initial velocity for rightward and leftward stimulation were averaged and segregated into 1°/s bins. Entire bar indicates total number of subjects in bin for both 60°/s and 150°/s stimulation. Black portion of bar alone indicates 60°/s drum velocity, and white portion alone, 150°/s drum velocity.

sight.[11] The subject's head was stabilized by a chin rest. Optokinetic nystagmus was induced by rotating the drum at either 60°/s or 150°/s. During the optokinetic stimulation the subjects were instructed to "look at the squares as they pass directly in front of you." During the periods of darkness the subjects were told to "look straight ahead." Subjects were encouraged at the beginning of each trial, but otherwise no other alerting maneuvers were used.

Horizontal eye movements were recorded by DC electro-oculography with miniature silver–silver chloride electrodes placed bitemporally. Vertical eye movements and blinks were registered by electrodes placed above and below the right eye. Eye position signals were amplified differentially (Tektronix 5A22 amplifier), low-pass filtered (3-dB point, 40 Hz), and then sampled at 100 Hz with 12-bit resolution by a laboratory computer.

Three identical tests, separated by rest periods of 5 minutes, were performed upon each subject. Each test consisted of four trials, each separated from the next by 2 minutes of darkness. The trials consisted of stimulation at drum speeds of rightward 60°/s, leftward 60°/s, rightward 150°/s, and leftward 150°/s. Calibration of eye position was performed at the beginning of each test by alternate viewing of one of two light-emitting diodes 40° apart.

In each trial optokinetic stimulation lasted for 60 seconds, and during each trial the lights were switched off at 12, 26, 40, and 60 seconds after the onset of optokinetic stimulation to "sample" the OKAN.[12] After the fourth OKAN sample, the lights remained off for 2 minutes. This arrangement of samples allowed us to obtain four values for OKAN initial velocity during the 1 minute of OKN stimulation.

Data Analysis. The velocity of every slow phase was determined by reviewing the eye position data upon a graphics monitor. The initial velocity of OKAN was obtained by determining the velocity and duration of every slow phase that occurred in the second second after the lights were switched off. The data from the first second were discarded. Because three tests were performed, each containing four samples for each trial, a total of 12 sample values were available for each velocity-direction combination. Although a few samples were discarded because of artifacts such as eye closure, we obtained, on average, 11 sample values from each subject. The value of the OKAN for each sample period was calculated by averaging together the velocity of every slow-phase segment in the second second, weighted by duration. The sample values in a given person for trials with the same speed and direction were averaged to produce the mean initial slow-phase velocity of OKAN. The variability of the initial velocity was quantified by calculating the coefficient of variation of the mean based on the 12 sample values.

The time constant of decay of OKAN was calculated from the profile of decay of slow-phase velocity during the first 30 seconds of the 2-minute darkness interval, excluding the first 2 seconds. The time constant was determined from the slope of the line that relates the log of the slow-phase velocity to time. The regression was obtained by the method of least squares, weighted by slow-phase duration. The individual time constants were averaged together, for both rightward and leftward stimulation, so that the summary value for the time constant reflected the mean of six trials/subject. In order to compare sampled values with nonsampled data, OKAN initial velocity was calculated from the y intercept of this regression. The decline of the slow-phase velocity also was fitted to a straight line for comparison with the exponential fit.

A symmetry measure of OKAN initial velocity, subsequently called directional preponderance, was calculated by taking the difference between the mean values of rightward and leftward initial OKAN velocity and dividing this value by their sum. This formula is the same as that used to quantify directional asymmetry of caloric responses. Another measure of symmetry, called difference, was calculated by subtracting rightward and leftward OKAN velocity. For the time constant data, preponderance and difference measures of symmetry were calculated in the same way.

RESULTS

OKAN Initial Velocity. Figure 1 shows the distribution of the values of OKAN initial velocity among the 30 subjects. These values were calculated from

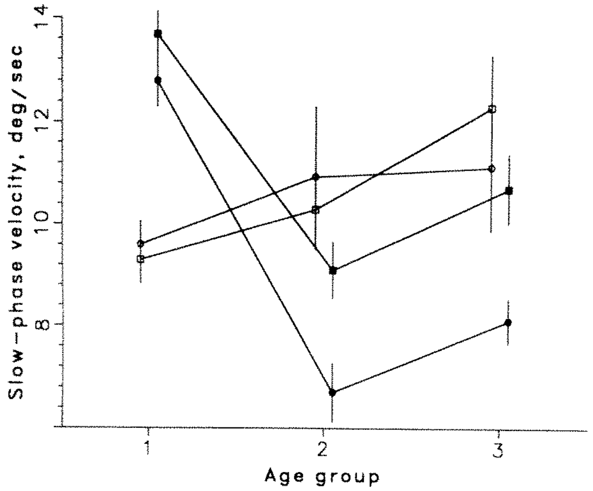

Fig 2. Mean initial velocity of optokinetic afternystagmus (OKAN) plotted for 12 subgroups that reflect combination of three age groups, two sexes, and two stimulus velocities (60°/s and 150°/s). Each point represents mean of ten responses, each of which was calculated from 12 measurements of OKAN. Squares indicate 60°/s stimulation, and circles 150°/s stimulation. Filled symbols indicate women, and open symbols men. Subgroups with same gender and stimulus velocity are connected with lines. Vertical lines indicate standard error of mean.

the mean of 24 samples/subject. The average initial velocity at 60°/s drum velocity was 10.9°/s ± 2.9°/s (mean ± standard deviation), and at 150°/s drum velocity, 9.9°/s ± 3.9°/s. The range of means of initial velocity considering rightward and leftward responses was 5.9°/s to 21.3°/s for 60°/s stimulation, and 3.8°/s to 22.2°/s at 150°/s drum velocity. The OKAN initial velocity calculated by fitting the decay of velocity to an exponential (six values/subject) was slightly greater and more variable than the OKAN initial velocity calculated from the multiple samples, being 12°/s ± 5.9°/s and 11°/s ± 5.2°/s for the 60°/s and 150°/s drum velocities, respectively.

Figure 2 shows the effects of age, sex, and drum velocity on the initial velocity of OKAN. Analysis of variance (ANOVA) using the variables age group, sex, and drum velocity showed a highly significant interaction between variables age and sex ($F = 133.9$, $p = .0001$). In particular, women in age group 1 had high initial OKAN velocity, and the comparison of the mean behavior of group 1 women (mean, 13.2°/s ± 2.1°/s) to the remainder of the group (mean, 9.8°/s ± 3.8°/s) showed a highly significant difference ($F = 14.9$, $p = .0004$).

Because of this interaction, ANOVA to examine the effect of age on OKAN was done separately for each sex. For women there was a highly significant decrease of OKAN associated with increasing age ($F = 22.9$, $p = .0001$). For men there was no significant effect ($F = 1.5$, $p = .22$).

Since the sampled paradigm allowed us to acquire rapidly 12 measurements of OKAN initial velocity, we were able to assess the intraindividual variability of OKAN. This was substantial. The group mean of individual coefficients of variation (CVs) was 0.35 ± 0.12 (range, 0.17 to 0.70) for the 60°/s stimulus and 0.39 ± 0.13 (range, 0.17 to 0.88) for the 150°/s stimulus. Women of age group 2 had the most variability ($CV = 0.47 \pm 0.16$), and men of age group 3 the least ($CV = 0.32 \pm 0.08$).

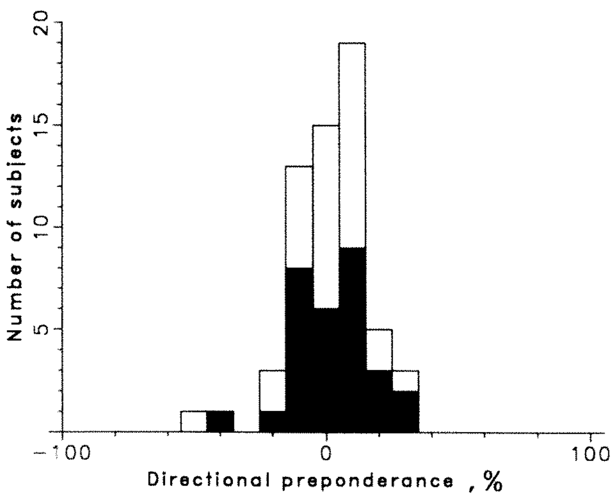

Fig 3. Histogram of distribution of directional preponderance of optokinetic afternystagmus initial velocity (rightward − leftward)/(rightward + leftward). These data are plotted as in Fig 1.

Statistical comparisons of the effects of the age, drum velocity, and sex variables on the CV were performed with ANOVA, as described above. Again there was a significant interaction between age and sex ($F = 6.1$, $p = .0036$). Analysis of variance made separately for each sex showed a significant increase of CV with age in women ($F = 5.6$, $p = .0062$). There was no significant effect of or interaction between age or drum velocity in men, and no effect of drum velocity on the CV in women.

Figure 3 shows the distribution of the values for directional preponderance of the OKAN for the 60°/s stimulus velocity. For the whole group the mean directional preponderance was −2.0% ± 14% with the 60°/s drum velocity and −5.0% ± 14% with the 150°/s drum velocity. The difference between responses to rightward and leftward stimulation was on average −0.47°/s ± 3.13°/s with 60°/s drum velocity and −0.94°/s ± 2.7°/s with 150°/s drum velocity. None of these means are significantly different from zero.

Time Constant. Figure 4 shows the distribution of the mean individual time constants calculated from the average of three trials for each combination of speed and direction. Statistical analysis with ANOVA, testing the age, drum velocity, and sex variables as described above, revealed no significant main effects or interactions. The mean time constant, calculated from six trials in each individual obtained by combining the two directions, was 11.3 ± 3.2 seconds for the 60°/s drum velocity

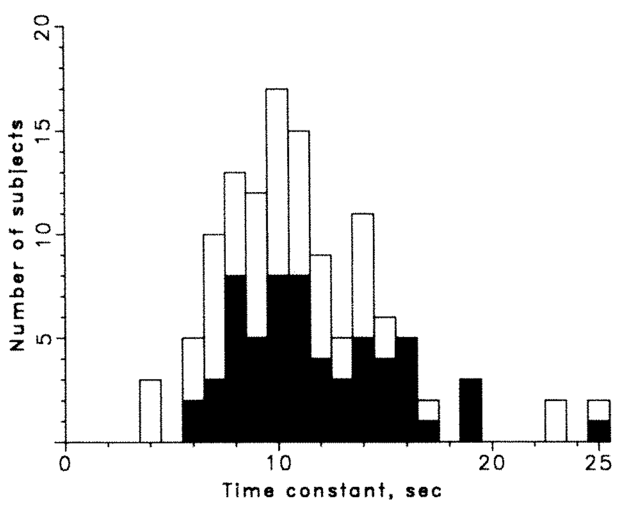

Fig 4. Histogram of distribution of time constants. For each subject, three measured time constants for each direction were combined into leftward and rightward mean values, which were plotted independently. Otherwise, format is as in Fig 1.

(range of means, 5.2 to 19.7 seconds) and 10.1±3.6 seconds (range, 3.5 to 19.3 seconds) for the 150°/s drum velocity.

The directional preponderance of the time constant, calculated in the same way as described for initial velocity, was 0.7% ±16.7% for 60°/s stimulation and −3.1% ±16.8% for 150°/s stimulation. The difference between the mean rightward and leftward time constants was 0±4.2 seconds for 60°/s stimulation and −1±3.9 seconds for 150°/s stimulation. As with initial velocity, none of these values are significantly different from zero.

We also compared the correlation coefficients of slow-phase velocity versus time for two methods of fitting the decay: logarithmic and linear. A total of 351 trials were available for analysis (12 values of the time constant for each subject; three of each combination of velocity and direction). Of these, 289 trials were better fit by an exponential, and 62 trials by a linear function.

DISCUSSION

To use OKAN initial velocity, time constant, and directional asymmetry as diagnostic factors in patients it is necessary to compare them with normal values. The sensitivity and specificity of such parameters for disease depend critically on the intrinsic variability of the normal population. Our data suggest that only 1) initial OKAN velocity and 2) directional asymmetry of initial OKAN velocity or difference can be measured quickly with an adequate precision such that registration of changes in these quantities might allow detection of vestibular lesions. We will proceed to discuss each measure in detail.

Initial Velocity. We found that the initial velocity of the OKAN in our 30 subjects for the 60°/s drum velocity was 10.9°/s±2.9°/s. This finding agrees with those of previous reports in which normal subjects were studied with use of similar stimulus velocities.[12-14] We noted that OKAN initial velocity calculated from the regression of the entire time course of the decay was greater by about 1°/s than the values calculated from the samples. This observation is explained by the intrinsic differences between these two methods of obtaining the initial velocity. The sampled measure represents the OKAN measured at time 1 to 2 seconds, while the regression method estimates the OKAN at time 0 seconds.

We also found that drum velocity of 150°/s produced about 10°/s of OKAN. No data are available for comparison at this high speed of stimulation. Although Simons and Büttner[15] reported higher values, their methods differed substantially from ours. They used velocities intermediate between 60°/s and 150°/s and reported the best response. Such intermediate velocities may produce an OKAN response greater than 10°/s.[16] Also, the best response, which they reported, does not include effects of intrinsic variability between trials that may lower the mean response, such as we report.

For the women, but not men, OKAN initial velocity showed a significant decline with age. This mainly reflected the tendency of women in group 1 (22 to 35 years of age) to have stronger OKAN than the rest of the population. The decline of OKAN in our subjects considered as a whole was numerically small. The larger effect of age on OKAN suggested by the data of Simons and Büttner[15] may reflect a greater sensitivity to age of the "best OKAN" obtained by the latter authors, as opposed to the "mean OKAN" measured by us.

Time Constant. The mean time constant for the OKAN decay in our 30 normal subjects was 11.3± 3.8 seconds. The range of the mean time constant (calculated from six trials/subject) was 5.2 to 19.7 seconds. These results are similar to those in Segal and Liben's report,[12] except the latter authors studied fewer subjects (six) and consequently reported a smaller range (4.4 to 11.1 seconds).

Lafortune et al[17] and Jell et al[13] found much larger mean time constants (about 22 and 49 seconds, respectively). We have no explanation for this discrepancy other than differences in method. In the previously mentioned studies, the time constant was obtained by fitting the decay of slow-phase velocity to two exponentials, rather than one. Such fits require fitting of the decay time-course to four variables rather than the two needed by a single exponential fit, and accordingly are more vulnerable to artifact introduced by noise. In consequence, such curve-fits may result in a spurious increase of the time constant of the second exponential. Other authors who reported smaller time constants[10,12] used single exponential fits.

Linear decay of OKAN has been observed in some species,[18,19] and it has been suggested that humans also might exhibit this behavior.[10,20] However, in our subjects the correlation coefficients of the slow-phase velocity upon time were predominantly higher for an exponential fit than for a linear fit. This finding is consistent with the conventional belief that OKAN reflects an exponentially decaying process. It is possible that at lower stimulus velocities the OKAN decay is more linear, as this pattern has been reported in rabbits and monkeys.[18,19]

Variability. Our study is the first to measure the variability of OKAN. In all subjects we found a large intraindividual variability of initial OKAN, amounting to a coefficient of variation of 35% for the 60°/s drum velocity. At the same time, we noted less interindividual variability, reflected by a smaller standard deviation than has been reported by others.[14] Consideration of this variability is important, as it allows one to infer how much significance should be attributed to measurements of OKAN initial velocity.

Another way of expressing this idea is to calculate how many measurements of OKAN initial velocity are needed to be 95% confident that the mean value is within ±25% of its true value. This can be calculated by the formula[21]

$$N = 4(\text{coefficient of variation})^2/(\text{confidence limit})^2$$

It follows that one should take eight initial velocity samples for each direction using 60°/s data and ten samples using 150°/s data to achieve this confidence limit. Alternatively, if only one sample for each direction is taken, as is the usual case in studies of OKAN, for the 60°/s drum velocity one can only be confident that the single OKAN measurement falls within ±70% of the true mean.

The difference between our results and those studies that found large intersubject variability is probably explained by differences in method. For example, Zasorin et al[14] reported that OKAN showed a large standard deviation amounting to 4.5°/s associated with a mean response of 6.3°/s. They also noted that two of 20 subjects did not show OKAN at all. These data, however, were obtained in a protocol in which only one trial of OKN was performed. Thus, trial-to-trial intrasubject variability might have accounted for their findings. Some of our subjects showed no OKAN on one or two individual trials, but showed a response for other trials.

Similar to initial OKAN, the time constant also showed a large CV, averaging 32%. In the same way as outlined above, we calculate that it requires seven measurements of the time constant to be 95% certain that the measured mean time constant is within 25% of its true value. In terms of testing time, approximately 2 minutes is required to obtain each time constant, and therefore it should require 14 minutes of testing, for each direction, to be reasonably confident that the OKAN time constant is correct.

Directional Preponderance and Asymmetry Measures. Few quantitative data are available on OKAN directional asymmetry. Ireland and Jell[9] suggest that normal OKAN is symmetric, but do not give numeric results. Zasorin et al[14] stated that four of their 20 subjects had no OKAN in one direction. As mentioned above, however, intrasubject variability might account for apparent intersubject variability.

Our data document that there is generally little difference in initial slow-phase velocity between leftward and rightward rotation. The mean of the right and left difference found in the 30 subjects was only −0.47°/s±3.13°/s. Two subjects had >6°/s of directional asymmetry, and we propose that values >6°/s (when 12 measurements are taken in each direction) should be considered abnormal. Directional preponderance, which is an alternative method of quantifying directional asymmetry, might be more sensitive to disease, because it is normalized to the magnitude of the response. One subject had more than a 30% directional preponderance, and we propose that a directional preponderance greater than 30% should be considered abnormal. As the limits of normal are a function of the reliability of the measure, if fewer trials of OKAN were obtained, the limits necessarily would become larger.

For the time constant, setting two standard deviations from the mean to be the criterion of abnormality, then a 33% directional preponderance or 8.4-second difference between the time constants should be considered abnormal. Larger limits would be necessary if fewer than three trials in each direction were taken.

Clinical Implications. Our data have important implications for the clinical evaluation of OKAN in humans. The main conclusions relate to intrasubject variability. In particular, because intrasubject variability is large, for the routine 60°/s drum velocity, eight measurements are necessary to obtain a reasonably precise estimate of the initial OKAN slow-phase velocity. Measurement of the directional asymmetry or preponderance of OKAN initial velocity may be a good indicator of vestibular dysfunction if it is measured with sufficient precision, and this is possible using the sampling technique.

On the other hand, the time constant of OKAN is unlikely to be a useful index of vestibular dysfunction. This is because, in clinical testing situations, it is impractical to obtain enough measures of the time constant to reduce variability of the mean to acceptable levels.

Further studies of OKAN in patients with unilateral peripheral lesions, using multiple measurements to obtain precision, are indicated to examine the question of the use of OKAN testing in diagnosis of vestibular lesions.

ACKNOWLEDGMENT — Cheryl Enger of the Wilmer Institute of Ophthalmology and the Department of Biostatistics helped with the statistical analyses.

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IMAGING CASE STUDY OF THE MONTH

GADOLINIUM-ENHANCED FACIAL NERVES: ACCOMPANYING BILATERAL ACOUSTIC TUMORS IN A PATIENT WITH NEUROFIBROMATOSIS

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INTRODUCTION

Gadolinium DPTA/dimeglamine is a paramagnetic compound currently being assessed as a magnetic resonance contrast material by the Berlex Company, a division of Schering AG, Berlin. Present use of the compound is limited to the cooperating centers evaluating its use for brain tumor evaluation.

The agent is injected intravenously in a dose of 0.1 mmol/kg. Magnetic resonance imaging is conducted 1 hour after contrast injection. Plasma half-life is 90 minutes. The material collects in the extracellular fluid within a tumor and produces an increased T1 signal.

PATIENT

A 28-year-old man had typical widespread cutaneous neurofibromas, symptoms of cerebral tumors, and bilateral sensorineural hearing loss. There was no evidence of facial nerve abnormality. He was placed on our gadolinium protocol for evaluation of the presence of multiple meningiomas and intracranial glial tumors.

RADIOGRAPHIC FINDINGS

On coronal MRI examination, in addition to the expected intracranial tumors (not illustrated), bilateral acoustic neuromas were rather prominently "enhanced" by the contrast agent. In the Figure, A, the larger lesion on the right fills the cerebellopontine angle cistern, compresses the adjacent pons, and extends laterally through the enlarged internal auditory canal to the fundus of the canal. The smaller, left-sided lesion is essentially intracanalicular and produces canal enlargement.

Peripherally on each side in the Figure, A, the geniculate and pregeniculate parts of the facial nerve also are enhanced.

On a more posterior coronal view (see Figure, B), a part of each acoustic tumor is seen. Peripherally, the descending portion of the facial nerve can be visualized from the horizontal portion all the way down to the stylomastoid canal area.

Both images in the Figure were obtained with a relatively T1-weighted spin echo pulse sequence (TR 600 ms, TE 20 ms) using a superconductive machine operating at 0.5 tesla. The slice thickness is 1 cm without interslice gap.

DISCUSSION

Previous studies have demonstrated that gadolinium DPTA does not enhance the normal temporal bone structures or nerves.[1] Increased signal has been noted in small vessels.

Daniels et al[2] have described 11 patients with masses in the cerebellopontine angle and internal auditory canal. Four of their patients had enhancement of the facial nerve in connection with lobular enlargements in the geniculate and horizontal parts of the nerve. No descending nerve enhancement was described in their article. In a second group receiving gadolinium but without cerebellopontine or internal auditory canal tumors, no facial nerve enhancement was observed.[2]

Only speculation is available regarding our patient, as surgical exploration of the facial canals was not carried out. Three possible explanations are forthcoming. The enhancement showed no enlargement of the affected facial nerves, so that only microscopic tumor may be suspected; however, no neurologic symptoms of facial nerve dysfunction were present. The mechanism of enhancement is probably due to the breakdown of the tumor-blood barrier.

The second possibility is that of edema of the facial nerves. Since gadolinium DPTA collects in extracellular fluid, one might expect enhancement of edema fluid produced by compression of the facial nerves in the internal canals. Such enhancement should be better seen in the delayed image because of the slower rate of contrast accumulation in the

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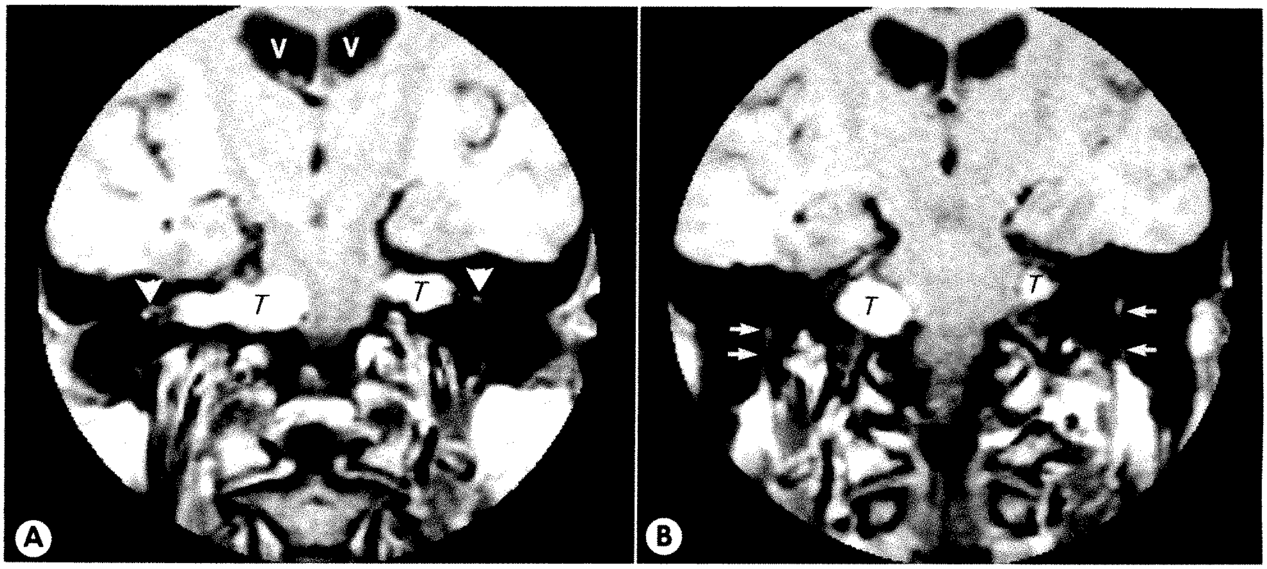

Coronal T1-weighted images (TR 600 ms, TE 20 ms). A) Image obtained 3 minutes after intravenous injection of gadolinium DPTA shows bilateral enhancement of acoustic tumors (T). Geniculate and pregeniculate parts of facial nerve also are enhanced bilaterally (arrowheads). V — lateral ventricles. B) One centimeter posterior to A, immediately after intravenous contrast. Enhancement of bilateral descending portion of facial nerve (arrows) is demonstrated, as is take-off of enhanced acoustic tumor (T) at cerebellopontine cistern.

edema by passive diffusion via the concentration gradient between the normal tissue and edema. As in our case, the enhancement of tumor was best demonstrated in the immediate postinjection period.

Third is the possibility of vascular enhancement along the facial nerves. This seems unlikely also, in the absence of facial nerve dysfunction and in consideration of the miniscule size of vessels in the facial canals. This also was not seen by Daniels et al.[2]

Since we have seen several tumors with immediate enhancement after intravenous contrast and without angiographic evidence of neovasculature, to us the breakdown of tumor-blood barrier seems to be most plausible, although the other mechanisms cannot be excluded completely.

Gadolinium DPTA not only collects within intracranial primary and metastatic tumors, but in animals has been shown to enhance other tumors, infarcts, and inflammation.[3] Infarction and inflammation were not suspected in our patient.

We do believe that facial nerve enhancement with gadolinium DPTA probably reflects the presence of neurofibromatosis and typically will be found with an acoustic tumor.

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PATHOLOGY CONSULTATION

ADENOMATOUS TUMORS OF THE MIDDLE EAR

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Primary adenomatous tumors of the middle ear are preponderantly benign, resectable lesions and arise from the mucosa (adenomas) or salivary tissue (choristomas). Malignant variants are ill defined, are not characterized histologically, and represent less than 10% of the adenomatous tumors. Their presence may be signaled clinically by facial nerve paralysis, invasion of bone, and chronic otorrhea.

Space-occupying, gland-forming tumors of the middle ear cleft may be classified into three groups: 1) secondary involvement of the middle ear by adjacent lesions, eg, ceruminomas of the external auditory canal and metastases to the temporal bone, 2) lesions of salivary tissue, eg, salivary choristoma and salivary gland tumors, and 3) primary adenomatous tumors (nonsalivary adenomas and adenocarcinomas). This report deals with the last two categories.

HISTOLOGY OF MUCOSA

The middle ear is anatomically continuous with the aditus ad antrum, mastoid antrum, mastoid cells, and eustachian tube, which connects the middle ear and mastoid air cells to the nasopharynx.[1]

The lining of the middle ear cleft is normally a thin mucosa, described by Tos[1] as a "strongly modified respiratory type." The height of the epithelium, shape of constituent cells, and their interrelationships are not uniform in all parts of the cleft.[1-3] There is a gradual transition from one type to another, progressing from the tubal orifice to the tympanic cavity and mastoid, with mucosal height decreasing as the distance from the tubal orifice increases. The anterior third of the tympanic cavity is lined mainly by a low pseudostratified cylindric epithelium, whereas one-, two-, or three-layered cuboidal epithelium is found in the middle, and a single-layered flat epithelium in the posterior third. A single-layered, flat epithelium also covers the antrum, mastoid process, and ossicles. Since 80% of children are estimated to have at least one bout of chronic secretory or acute purulent otitis media, the adult ears' mucosa shows consequent modifications from the normal.[1,4] The majority of cells are nonciliated, but tracts of cilia-bearing cells can be followed in the middle ear cavity to the orifice of the eustachian tube.[1,2] In air-filled ears, little secretory activity is found. The distribution and density of goblet cells vary according to the location in the cleft and also with the age of the individual.[1,4]

Notably, a distinct lamina propria is found only in the pharyngeal part of the eustachian tube.[1-3] This lamina decreases in thickness toward the tympanic cavity, especially in the posterior parts of the middle ear. Tubuloalveolar seromucous glands, numbering about 90, not unlike those in the nasopharynx and nasal cavity, are normally found in the lamina propria of only the pharyngeal (cartilaginous) part of the eustachian tube.[1,2] The tympanic cavity, antrum, and mastoid normally do not contain seromucous glands. Any glands, therefore, in the middle ears of children or adults are presumed to be local sequelae to a pathologic action in the middle ear cleft.[1,4]

SALIVARY TYPE LESIONS

Since the normal mucosa of the middle ear is devoid of salivary type seromucous glands, their presence is explained by either a stimulated morphologic and functional differentiation of surface epithelium or a teleologic ectopia associated with developmental errors around the proximal part of the second branchial arch. The findings with salivary choristomas support the second possibility.

Salivary choristomas have been reported in various locations in the middle ear, but have been related most often to the seventh nerve and with ossicular abnormalities.[5,6] Developmental disorders of the external ear and face also may be present. There is a marked left ear preponderance. On occasion, the lesions have been bilateral. Age of patients at time of diagnosis has ranged from 5 to 52 years.[5,6] Deafness is the most consistent symptom. Clinical findings include a middle ear mass and a conductive hearing loss.

The choristoma is a somewhat lobulated and firm mass, usually located in the posterosuperior tym-

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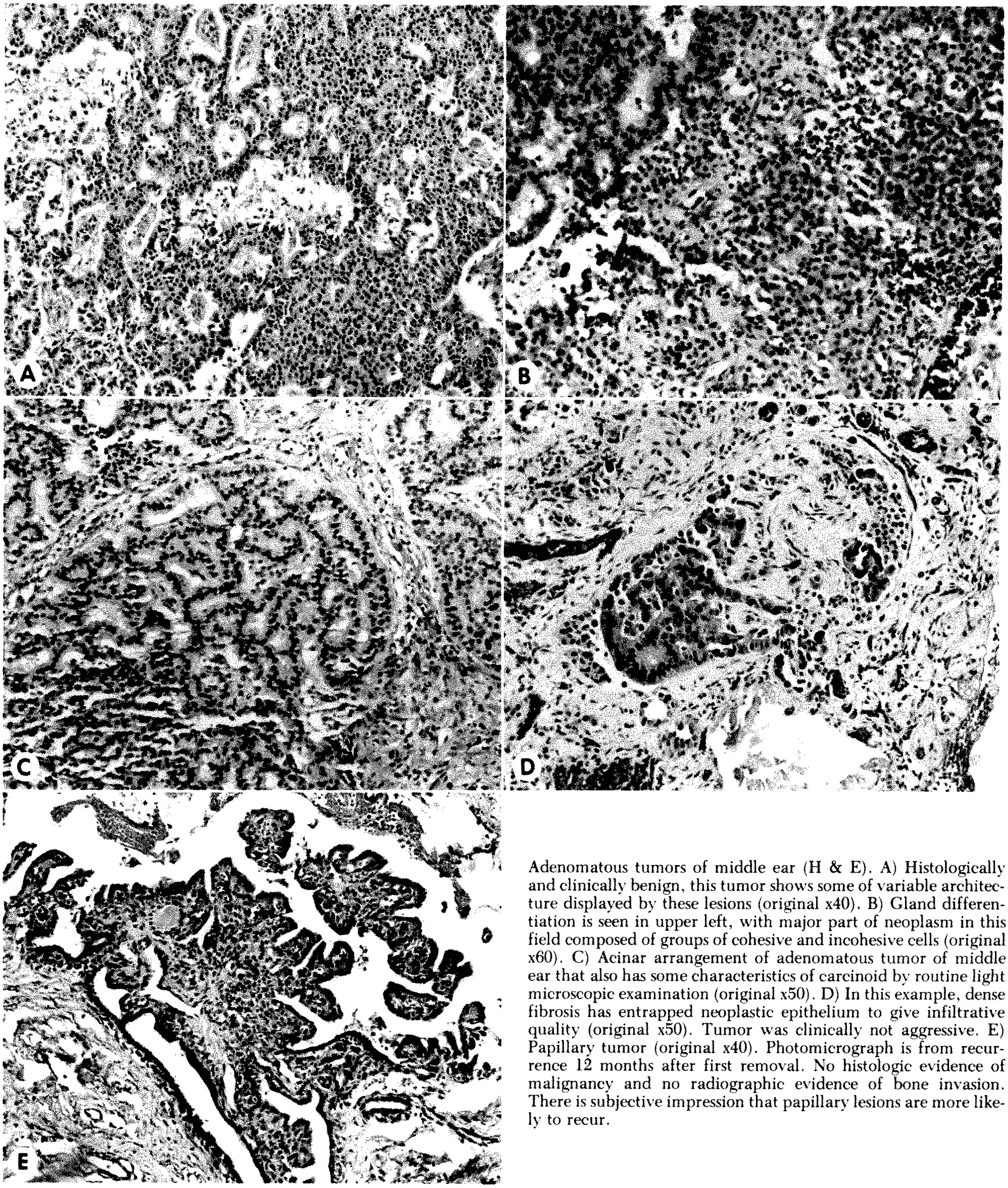

Adenomatous tumors of middle ear (H & E). A) Histologically and clinically benign, this tumor shows some of variable architecture displayed by these lesions (original x40). B) Gland differentiation is seen in upper left, with major part of neoplasm in this field composed of groups of cohesive and incohesive cells (original x60). C) Acinar arrangement of adenomatous tumor of middle ear that also has some characteristics of carcinoid by routine light microscopic examination (original x50). D) In this example, dense fibrosis has entrapped neoplastic epithelium to give infiltrative quality (original x50). Tumor was clinically not aggressive. E) Papillary tumor (original x40). Photomicrograph is from recurrence 12 months after first removal. No histologic evidence of malignancy and no radiographic evidence of bone invasion. There is subjective impression that papillary lesions are more likely to recur.

panum, that varies in size from 5 mm to a mass filling the tympanic cavity. An attachment to a dehiscent part of the horizontal facial nerve often is noted.[5] In most cases, there are developmental abnormalities of the ossicles, most often of the stapes, with the incus and malleus following in frequency, respectively. The oval window may be absent.[5,6]

The lesions grow slowly, if at all, and produce no morbidity except for the initial loss of hearing and that related to biopsy/excision of the mass, eg, temporary facial weakness. Their nonprogressive, benign character and frequent intimate relation to the facial nerve should caution the surgeon.

Well-formed serous and mucous acini in a random or approximately lobular formation characterize the histologic appearance. Ducts may be absent, but small mucinous cysts may be present. A number of the reported examples also have contained a component of fibroadipose tissue.

The possibility of a salivary neoplasm arising from choristomatous middle ear tissue is remote. Only one (a mixed tumor) has ever been recorded.[5]

ADENOMATOUS TUMORS

Primary, nonsalivary adenomatous tumors of the middle ear have a presumed origin from surface epithelial progenitors. Although these tumors are usually benign, with an indolent biologic course, more locally aggressive and even lethal forms exist.[7-12] It is nearly impossible, however, to cull the latter from published cases. This is due to several factors: 1) confusion with ceruminous neoplasms invading the middle ear, 2) a decided tendency by early authors to classify all adenomatous tumors of the middle ear as adenocarcinomas, 3) poor or even no photomicrographic documentation, and 4) an absence of histopathologic criteria enabling the pathologist to identify malignant adenomatous tumors objectively.

Since there is a histologically undefinable separation in the biologic gradient from benign to malignant adenomatous tumors of the middle ear, resort has to be made to ancillary clinicoradiographic findings, eg, preoperative seventh nerve paralysis and bone invasion.

To Hyams and Michaels[7] goes the credit for the first comprehensive clinical gross and microscopic assessment of these tumors. The chief complaint of most patients is a decreasing unilateral hearing acuity from 1 month to several years in duration. A sense of fullness in the ear and tinnitus are other symptoms. A history of chronic otitis media usually is not elicited. The tympanic membrane is intact more often than not, and the tumor may produce a bulge in the membrane, with a clinical misdiagnosis of paraganglionic tumor. Intraoperatively, a firm to rubbery nonvascular mass may fill the middle ear space and extend into mastoid spaces or be localized to various areas of the middle ear (promontory, hypotympanum, etc). Regardless of size, most of the tumors have been described as tightly adherent to the middle ear mucosal surface. A similar adherence to the ossicles and tympanic membrane is found where these structures are involved. Destructive invasion of bony walls is not a feature of the considerable majority of the tumors and, if present, signifies the likelihood of carcinoma.[12]

An adenomatous pattern is always conveyed by light microscopy. In this pattern, three principal growth architectures are displayed: 1) glandular or pseudoglandular, arranged in trabeculae, back-to-back array, or as glands separated by stroma, 2) sheets, nests, or cords of compact to incohesive, relatively uniform cells, 3) papillary or papillocystic (see Figure). Any of the three may be preponderant, but the papillary form is the least common. If there is a prototype, it could be a tumor showing a combination of the first two architectures. A stromal accompaniment may be minimal or conspicuous and is fibrous or myxofibrous, at times with chronic inflammatory cells. Entrapped glands and cells in the stroma may give the impression of invasion by the glands. The tubules or glands are lined usually by a single layer of cells that are cuboidal or low-columnar. The double layer of ceruminous glands is not present, and although many of the cells have an eosinophilic, sometimes abundant, cytoplasm, it is not apocrine in type. Optically clear cells may be present, but not in a hypernephroid appearance. The non–gland-forming cells are one of the characteristic features of the adenomatous tumors having a benign clinical course. They are uniform, are oval to polygonal, and have hyperchromatic nuclei. The nuclei may manifest various degrees of pleomorphism, but the cytoplasm and cell borders are distinct. Mitosis in any cell type is unusual. Mucicarminophilic and/or colloidlike inspissated protein material can be seen in lumens. Intracellular mucin rarely is found.

A number of the adenomatous tumors display a carcinoidlike appearance by light microscopic study, and single case reports based on a demonstration of argyrophilia, formaldehyde fluorescence, electron microscopy, or all three techniques have strengthened the carcinoid thesis.[13,14] It should be noted, however, that none of the procedures are conclusive. Argyrophilia is not specific for a neuroendocrine differentiation, and membrane-bound secretory granules of a mucinous character can be argyrophilic. Electron optic study of the nonadenomatous mucosa of the middle ear has not demonstrated cells with neuroendocrine characteristics, despite a variety of cytoplasmic organelles. Whether or not neuroendocrine differentiation is present in adenomatous tumors of the middle ear has little bearing on biologic behavior. A foregut endodermal origin of the middle ear may be responsible, but local microenvironmental stimuli or needs are more likely the initiators of neuroendocrine differentiation in cells capable of this modification.

Review of reported cases of adenomatous tumors of the middle ear indicates that despite histopathologic ambiguity, the great majority are resectable, seldom recurrent, nonlethal lesions. The tumors afflict both sexes equally and over a wide age range (14 to 80 years), with a mean age at diagnosis of 40 years. In 56 patients classifiable as having benign adenomatous tumors, follow-up periods have extended from 1 to 24 years (median, 4 years).[8-10] The tumor was resectable in every patient, nearly equally divided between transtympanic or postauricular simple excision and tympanomastoidectomy or radical mastoidectomy. One patient underwent temporal bone resection. Five patients (9.6%) had recurrences (one with two), and all were controlled by local reexcision. No patient has died as a consequence of the tumor. Documentation of radiographic findings, unfortunately, is less complete than that dealing with the histologic appearance and operative procedures. Less than half of the case reports give this information. In the remainder, erosion of bone is not mentioned or is specifically denied.[8]

Malignant adenomatous tumors (adenocarcinomas) have been reported, but unfortunately not illustrated. Pallanch et al[11] record three cases, and Shuller et al,[15] two, one of which was their own. Time intervals, when noted, to death from "local invasion" were 2 months in two of the patients and 11 and 13 years in the others. Of these, we have no histologic information, but the clinical findings of bone destruction, preoperative seventh nerve paralysis, and chronic otorrhea bespeak a more aggressive lesion than the majority of adenomatous tumors of the middle ear.

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LETTERS TO THE EDITOR

To the Editor:

The results of the retrospective review of Drs Robert Jackson and Dale Rice (Blood Transfusions and Recurrence in Head and Neck Cancer, *Ann Otol Rhinol Laryngol* 1989;98:171-3) are frightening. The outcomes are so grossly and statistically different that transfusion seems contraindicated under any circumstance. We are, however, presented inadequate information to use to compare "apples and oranges." Additional factors in the transfusion-nontransfusion decision probably bias this report.

Specifically, what were the indications for transfusion? What differences in patient characteristics, nature of disease, and ease of surgery would cause one patient to require blood whereas another with the same stage of disease did not? Were there preoperative differences in immune status, nutritional status, or tumor biology that simultaneously could have predisposed to recurrence and the necessity for transfusion?

Unless these questions are addressed, this study will be misused to legitimize an argument against transfusion when the identical conclusion might (but not necessarily) be reached in a retrospective review of other dichotomous events in patient care (such as left versus right subclavian vein catheterization).

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To the Editor:

As pointed out in our references,[1-4] we were not the first to observe the adverse effect of transfusion on recurrence rate in cancer patients. An additional recent report has reached the same conclusion for prostatic cancer.[1] Thus, this phenomenon seems to apply to nearly every organ site studied.

It also is known that blood transfusions depress cellular immunity.[2,3] Our patients showed no difference between a single unit of blood (admittedly an uncommon amount to be given) and multiple units. A recent study by Blumberg et al[4] reached the same conclusion, but also found that transfusions of three units of packed cells or less resulted in no increased risk. A presentation at the spring meeting of the American Society for Head and Neck Surgery analyzed 16 variables and their relationship to recurrence and found only blood transfusions and margin status to be statistically significant.[5]

Blumberg et al[4] also found an accelerated rate of recurrence in transfused patients. Unfortunately we did not tabulate those data systematically, but are currently gathering these data. However, a casual comparison of the patients on whom we incidentally had the data revealed time to recurrence to be half as much in transfused patients as in nontransfused patients. The number of patients is small.

We find surgical skill difficult to quantitate, especially in a residency training program in which the senior surgeon is first assistant. In all cases the tumor margins were clear. If other investigators confirm our findings and those of Blumberg et al,[4] it would seem prudent to minimize blood loss and to use packed cells instead of whole blood.

Further work needs to be done.

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To the Editor:

I read with interest the article by Furman et al (Alternate and Simultaneous Binaural Bithermal Testing: A Comparison, *Ann Otol Rhinol Laryngol* 1988;97:359-64). Since it had been accepted for publication presumably by peer review, I was surprised that it was published without editorial comment or critique.

The statements made indicate that response to the simultaneous binaural bithermal (SBB) stimulus is not as valuable as previously described.[1] Since the findings and conclusions were markedly different from mine after my 20 years' experience, I undertook a closer examination of the study.

First, the authors selected the receiver-operator characteristic (ROC) methodology. This statistical method is valuable when dealing with two independent variables such as the SBB and the alternate binaural bithermal (ABB) stimulus, but requires diagnostic truth against which to measure these variables.[2] In this instance the ABB was used as "diagnostic truth" to distinguish between a "healthy" population and the patient populations. The use of the word healthy and the fact that there is no gold standard flies in the face of ROC methodology, in which "diagnostic truth must be known in order to score the quality of each decision."[2]

Second, since the ROC methodology was selected, a numerical value needed to be assigned to each variable. To achieve this the authors developed "two nonconventional methods for evaluating the simultaneous test in a quantitative fashion." "Each of the nonconventional methods . . . required measuring the peak slow component velocity attained." They computed the difference between the average of the peak slow component velocities generated during warm and cool simultaneous irrigations and then presumed that a reduced vestibular response increases this difference. Another presumption was that the directional preponderance altered the average of the cold and warm responses. These presumptions were never alluded to in any publication and clearly have no foundation in the physiology of the vestibular system. This manipulation of the data revealed a basic lack of understanding of the functioning of the vestibular system and certainly influenced the interpretation of the information.

I believe the design of the study to be flawed in the selection of the statistical analysis and the subsequent manipulation of the data to assign a quantitative value. Once one is familiar with the physiology and pathophysiology of the SBB, its usefulness in clinical diagnosis is clear.

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To the Editor:

We were surprised and dismayed to read the comments of Dr Brookler concerning our study of alternate (ABB) and simultaneous (SBB) binaural bithermal caloric testing. In order to set the record straight, we would like to relate the following sequence of events. Our study questioned the validity and usefulness of Dr

Brookler's long-standing contentions regarding simultaneous caloric testing. Prior to sending the manuscript to the *Annals* in March 1987, and before its formal review process, we sent the manuscript to Dr Brookler for his comments. He provided insightful, helpful criticisms that were included in the paper. He saw the manuscript twice before we submitted it to the *Annals* and, in fact, our manuscript was revised twice on the basis of Dr Brookler's excellent suggestions at that time. He declined mention in the acknowledgment section of the paper.

Dr Brookler states in his letter, received 9 months following publication of our work, that the ABB "was used as 'diagnostic truth' to distinguish between a 'healthy' population and the patient populations." This is untrue. The ABB was not used to determine either the health or the normality of any of our subjects. This determination was made independently of the tests being evaluated as per receiver-operator characteristic (ROC) methodology.[1] Dr Brookler correctly indicates that a "gold standard" is required to evaluate the quality of a decision. However, as pointed out by Metz,[1] "The definition of truth is ultimately a philosophical issue, of course, and operational standards for diagnostic truth must be established for the purposes of evaluation analysis." As stated in our paper, the lack of a gold standard limits the implications of our study beyond an evaluation of the abilities of the two tests to distinguish between a patient and a healthy population. However, ROC is the appropriate statistical methodology in that we wished to compare the relative abilities of two clinical tests.

Dr Brookler correctly points out that our methods of quantitating the SBB were never alluded to in any (of his) publications. However, our methods certainly are based on a detailed understanding of the physiology of the vestibular system. The implication that our data were "manipulated" is simply untrue and pejorative. Moreover, Dr Brookler's contention that our study "revealed a basic lack of understanding of the functioning of the vestibular system" is deceitful and misleading. There is a universal lack of understanding of the anatomic/physiologic basis of this aspect of the vestibular system that is due to the unavailability of data from animal studies of the response to SBB, rather than any misconceptions of the authors.

Dr Brookler states that the usefulness of the SBB "in clinical diagnosis is clear." Our study failed to support his claim.

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To the Editor:

In my article entitled "Medical or Surgical Complications Related to the Nucleus Multichannel Cochlear Implant" (*Ann Otol Rhinol Laryngol* 1988;97[suppl 135]:8-13), I inadvertently stated that reporting cochlear implant complications to the manufacturer or to the US Food and Drug Administration (FDA) was not mandatory. In fact, because the manufacturer is responsible for monitoring the status of the device's premarket approval, it must report complications related to the Nucleus 22 Channel Cochlear Implant System to the FDA on an annual basis. Physicians performing the 22-channel implant procedure should report medical and surgical complications to the manufacturer.

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BOOK REVIEWS

An Atlas of Head and Neck Surgery

John M. Loré, Jr. 3rd ed. Hard cover, illustrated, indexed, 1,186 pages, 1988. WB Saunders, Philadelphia, $125.

The previous two editions of this atlas were published as two separate volumes, and they were regarded highly as a comprehensive review of head and neck surgical procedures. The third edition, in one volume, represents an update of this monumental work. Computed tomography and magnetic resonance imaging have been included with expansion of chapters dealing with myocutaneous flaps, thyroid and parathyroid surgery, compression plates for facial bone reconstruction, and voice prostheses, just to name a few. A brief discussion on chemotherapy highlights the major recent advancements in this area.

The chapters are arranged in a logical fashion, most often with an initial explanation of the topic's basic principles. Each procedure is demonstrated in a series of well-organized illustrations with an accompanying step-by-step, concise description, brief delineation of the important points, and a review of possible complications. Some illustrations show their age (eg, using Penrose drains instead of closed suction tubing), but their anatomic accuracy and excellent demonstration of the described procedures make up for this minor drawback. I also would have appreciated further discussion on trapezius myocutaneous flaps and the use of microvascular free flaps for reconstruction. The bibliography for each chapter is extensive and has been updated appropriately.

This book represents one of the most complete atlases on head and neck surgery to be published. Dr Loré's direct discussion of each topic, coupled with his easily understood description of procedures and clear illustrations, results in a novice surgeon's delight. This edition should be included in the library of every otolaryngology resident as a quick and accurate source of head and neck surgery procedures.

Mark S. Persky, MD
New York, New York

The Larynx: A Multidisciplinary Approach

Marvin P. Fried, editor. Hard cover, illustrated, indexed, 640 pages, 1988. Little, Brown and Company, Boston, $95.

The stated purpose of this book is to bring together the entire "spectrum of laryngology . . . in one source for the generic laryngologist," and Dr Fried has succeeded admirably. A wide range of experts on the larynx have been chosen to present their particular expertise on various topics in laryngology. The book is divided into 12 sections, starting with basic embryology, anatomy, and physiology and proceeding through diagnosis, pediatric laryngology, the voice, inflammatory laryngeal disorders, laser laryngoscopy, sleep apnea, trauma, deglutition, benign and malignant neoplasms, radiation therapy, oncology, and rehabilitation. The chapters are well balanced, with a clear, easy-to-understand text and illustrative diagrams, radiographs, and tables. The rationale and contraindications for each treatment are presented in a straightforward manner, and a significant bibliography is available for further reference. This book is not a surgical atlas, but that is not its stated purpose. It would be a good addition to any otolaryngology–head and neck surgery library.

Stephen G. Rothstein, MD
New York, New York

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PROMOTION OF PATIENT APPOINTMENT COMPLIANCE IN INDIGENT PEDIATRIC MEDICAL CARE BY USE OF A MICROCOMPUTER

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A computerized system for appointment scheduling, medical record keeping, medical billing, patient tracking, and epidemiologic data generation was developed and applied in an indigent pediatric otologic clinic. Functions used to augment appointment compliance are 1) notifying the referring physicians, agencies, and health department coordinators of failed appointments and sending medical information on the attended appointments, 2) listing patients who failed appointments, 3) production of mailings for failed appointments, 4) automatic rescheduling of failed appointments, and 5) automatic calculation of patient attendance ratios. The attendance ratio can be used to help identify patients for referral to social service workers and to implement rewards designed to promote medical compliance. The automatic rescheduling of failed appointments resulted in 21% of new patients and 30% of return patients above controls returning for a medical visit. The recalled patients had a much lower economic status than our average clinic patient, ie, the system was effective in reaching the target population.

KEY WORDS — audiology, compliance, computer, medical records, otology, pediatrics.

INTRODUCTION

Patient medical compliance is one of the most serious problems in health care delivery. Sackett and Snow[1] have found that 50% of appointments initiated by health care professionals are missed by the patient and that approximately 50% of patients attending appointments do not comply with long-term medical regimens. Appointment compliance for pediatric preventive care may be higher.[1] However, families of lower socioeconomic status have been found to have a significantly poorer rate of appointment attendance than families with a higher socioeconomic status.[2] Parrish et al[3] reported the appointment failure rate in a pediatric psychiatric clinic serving indigent patients to be 58%. The compliance rates are even lower for children with an asymptomatic disorder or those referred for preventive care. Hardy[4] found that only 32.5% of patients referred for medical follow-up after auditory screening at school attended their visit.

This paper will present methods of increasing patient medical appointment compliance in an indigent pediatric otology clinic serving the Mid-South region of western Tennessee, northern Mississippi, and eastern Arkansas. This region represents one of the poorest areas in the nation, with 25% of all individuals living below the poverty level.[5] Availability of health care is a major problem. Most area public health care centers are understaffed and have a 35% to 45% appointment failure rate for their pediatric patients (Table 1). This very high appointment failure rate has a profound impact both on health care delivery and on the economic viability of clinics that already suffer from discounted Medicaid payments and a large medically indigent population that is not covered by any third party reimbursement system.

TABLE 1. MEDICAL COMPLIANCE IN VARIOUS PEDIATRIC CLINICS IN SERVICE AREA

Clinic Name	*No. of Scheduled Appointments for Year*	*Failed Appointments*		*No. of In-House Social Service Workers*
		No.	*%*	
Center for Developmental Disabilities				
Pediatric otolaryngology clinic*	1,701	507	38*	0
Otolaryngology high-risk referrals†	288	186	36	0
Newborn Center infant follow-up clinics§	2,000	900	45	1
Shelby County Health Department pediatric clinics§	71,400	28,400	40	0
Memphis Health Center pediatric clinics§	18,700	3,700	35	0
Lake County Health Care, Inc	17,715	7,086	40	0

*Baseline data.

†Initial referrals from newborn high-risk registry for auditory evaluations.

§Retrospective data rounded off to nearest 100 by data-gathering agency.

From the Department of Otolaryngology and Maxillofacial Surgery (Kavanagh), Boling Center for Developmental Disabilities (Smith, Golden), and the College of Allied Health (Hinkle), University of Tennessee, Memphis; and the College of Social Work, University of Tennessee, Knoxville (Tate). Funded by grants from the Maternal and Child Health Agency, Bureau of Health Care Delivery and Assistance, Department of Health and Human Services MCJ-473808; Blyth Software, Inc, Foster City, Calif; and the University of Tennessee Apple Seed Program.

REPRINTS — Kevin T. Kavanagh, MD, Dept of Otolaryngology, University of Tennessee, 956 Court, Rm B224, Memphis, TN 38163.

There are many strategies that can be used to increase appointment attendance. The most commonly used is to increase the appointment availability to the patient, not only by reducing medical and transportation costs, but by providing effective case management and social service. Although highly effective, social service/case management techniques cannot possibly address all the families who have poor appointment compliance, for in many clinics this amounts to hundreds of families per month (Table 1). Patient and family education is also very important at the time of referral (orientation statement), as are appointment prompters (reminders). The use of postcards to remind patients of their appointments has been found to increase total appointment attendance 11% to 25% compared to controls.[6-9] Reminders delivered by phone have produced mixed results, with several studies reporting a 10% to 19% increase in total attendance compared to controls,[8,10,11] and others finding no significant difference.[12,13] Behavioral techniques (based upon patient appointment attendance) involving reduction in patient waiting time, financial penalties, and eligibility to participate in lotteries also have been shown to be effective in augmenting medical compliance.[3,14,15]

One also must consider the complex educational and sociologic factors ingrained into the various cultures from which patients come. Short communications by phone or a few home visits from "foreign" health care workers are unlikely to change these factors. Glogow[16] compared several interventions designed to augment appointment compliance and concluded that it was not the information conveyed but the perception of caring on the part of the health care worker toward the patient that was the most important factor. It should be noted that many interventions designed to motivate families to seek health care actually may have a negative effect. Letters may be viewed as confrontational and be less effective than postcards. For example, Boswell et al[17] reported a negative effect using letters to reschedule psychiatric patients who failed their medical appointments. Patient acceptance of the appointment is also dependent upon the acuteness of the illness, as well as educational and sociologic factors that determine the ability of family members to comply without professional intervention. An increase in family contacts by mail, phone, or home visits will heighten the perceived importance of the medical appointment and lead to an increase in parental compliance. Patient medical compliance may be increased by a two-pronged attack. The first is to reduce the barriers to health care, and the second is to increase the perceived importance of the health care visit so that the patient or parent will be motivated to overcome these barriers.

In an attempt to mitigate the problem of poor patient appointment compliance, the University of Tennessee, Memphis, has developed a computerized patient management system. The system currently is used to schedule appointments, store medical data, perform epidemiologic and demographic studies, and to manage patient medical appointment compliance. This report will outline a protocol for use with the patient management system and discuss the system's effectiveness in recalling patients who have failed to attend their medical appointments.

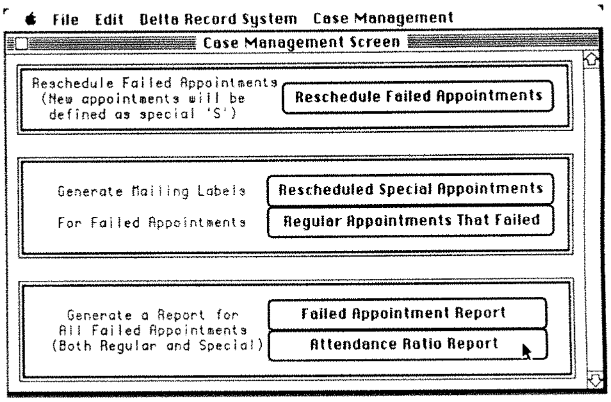

File
Edit
Delta Record System
Case Management
Case Management Screen
Reschedule Failed Appointments (New appointments will be defined as special 'S')
Reschedule Failed Appointments
Generate Mailing Labels For Failed Appointments
Rescheduled Special Appointments
Regular Appointments That Failed
Generate a Report for All Failed Appointments (Both Regular and Special)
Failed Appointment Report
Attendance Ratio Report

Fig 1. User interface of patient management system.

METHODS

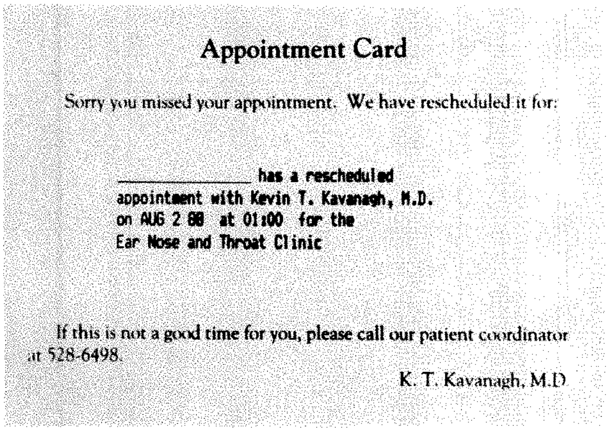
In order to evaluate the effectiveness of the patient management system in augmenting appointment compliance, a prospective study was performed to determine the impact that automatic rescheduling of failed medical appointments has on subsequent patient attendance.

Clinical Setting. This study was conducted at a pediatric otolaryngology clinic with an average baseline patient attendance rate of 62%. Seventy-one percent of the patients were black, and 59% were from families with single parents. The average yearly income of the families being served was $9,724. The majority of families were from inner-city Memphis. Many of the medical visits were for newborn auditory screening.

Hardware and Software. A Macintosh Plus with a 20-megabyte hard drive was used for the initial part of the project. This system was upgraded to a seven-terminal multi-user network during the second half of the study.

The software used to implement the project was the Delta Patient Management/Billing System, a multi-user relational data base written in Omni 3+. The program is a turnkey application that uses screen buttons and menus for a user interface (Fig 1). It has appointment scheduling, medical data storage, medical billing, and patient tracking capabilities. The patient tracking functions include

1. Generation of appointment reminder postcards and downloading of mail-merge files.
2. Calculation of appointment attendance ratios.



Appointment Card

Sorry you missed your appointment. We have rescheduled it for:

______________ has a rescheduled
appointment with Kevin T. Kavanagh, M.D.
on AUG 2 88 at 01:00 for the
Ear Nose and Throat Clinic

If this is not a good time for you, please call our patient coordinator at 528-6498.

K. T. Kavanagh, M.D

Fig 2. Postcard prompter used to recall patients who have failed their appointments.

3. Listing of patients who have failed their appointments.
4. Notification of referrers on whether the patient attended or failed the appointment.
5. Automatic rescheduling of patients who have failed their appointments.

The Delta Project's Patient Management/Billing System is shareware (free of charge to federal and state government projects and institutions, and to nonprofit indigent care clinics) that can be downloaded from the Delta Medical Shareware Forum on MacNet (Connect, Inc, Cupertino, Calif).

Clinical Protocol. The patient management/billing system was evaluated over a 12-month period. All patient appointments were defined as attended, failed, or canceled; and as new, return, or special. A canceled appointment was defined as an appointment canceled by the patient on or before the clinic visit date. A new appointment was defined as an appointment given to a patient who had never attended an ear, nose, and throat clinic visit. A return appointment was defined as an appointment given to a patient who had attended at least one ear, nose, and throat clinic visit. A special appointment was defined as a rescheduled failed appointment.

Four to 6 days before each clinic visit, all patients were sent a computer-generated appointment reminder (prompter) postcard that listed the appointment date, time, clinic doctor, and appointment type. Patients who failed to attend their medical appointments were divided into control and experimental groups based on the month of attendance. The experimental group was rescheduled by the computer for another appointment in 2 to 3 weeks, the control group in 6 to 7 weeks. Patient attendance at any otolaryngologic clinic held during weeks 1 through 4 and weeks 1 through 8 (measured from the date of the original failed appointment) was determined for all groups. All comparisons involving experimental and control groups were for an equal time span. Patients in both groups could attend at any time within this time window and be counted as having attended. If a patient canceled the rescheduled appointment, the next appointment was still defined as a rescheduled failed appointment for income analysis. If a patient canceled the rescheduled failed appointment and attended a clinic visit more than 4 weeks after the original failed appointment, the patient still was classified as failed in the 1- to 4-week analysis. A separate analysis of the attendance data for the last 4 weeks was not done, since some of the patients in the control groups would attend in the first 4 weeks (on their own), making their rescheduled visit during weeks 6 and 7 unnecessary.

Both groups received a computer-generated postcard (Fig 2). A yellow card was chosen, because people tend to remember colored material more than white.[18] These notifications were sent 1 to 2 weeks before the scheduled clinic appointment (just after the failed appointment for the experimental group and after a 1-month delay for the control group). Four to 6 days before the appointment, the patients were sent the standard appointment reminder postcard. Rescheduled failed appointments were defined as "special" by the computer, and if the patient failed, he or she was not rescheduled a second time. Rescheduled failed appointments and canceled appointments were not used in the calculation of the patient's clinic attendance ratio (number of total attended visits divided by number of total attended plus failed visits).

The time schedule for the management system was as follows. During week 1, on Monday, patients with failed appointments from the previous week (experimental group) and the fifth previous week (control group) were listed and automatically rescheduled for the following week (week 2). Postcards telling the patients of their rescheduled appointments were mailed. On Thursday/Friday, clinic appointment reminder cards were sent to all patients with appointments scheduled for the next week (week 2). These cards were timed to arrive 3 to 5 days before the scheduled appointment.

During week 2, on Tuesday and Thursday, an ENT clinic was held. The attendance ratio report was generated for all patients. Patients with a history of poor medical compliance were referred to social service workers.

The above cycle was repeated. At the end of the month, referrer reports were mailed, sending medical and attendance information to referring doctors, agencies, and the health department coordinator. Patient attendance rates were determined for the clinic. These rates aid in the determination of the maximum number of patients who can be scheduled for a clinic.

A portion of the new patients who failed to attend within a period of 2 months from their initial

TABLE 2. ATTENDANCE RATES WITH USE OF POSTCARD RESCHEDULING TECHNIQUE FOR WEEKS 1 THROUGH 4

	No. of Patients		
	New	*Return*	*Total*
Control			
Attended	5	16	21
Failed	52	74	126
Total	57	90	147
Experimental			
Attended	19	51	70
Failed	43	57	100
Total	62	108	170
χ^2	p<.0030	p<.0001	p<.0001

failed appointment were contacted by letter, and a home visit was conducted.

Three hundred seventeen patients were rescheduled by means of a postcard. A total of 159 patients were in the control group and 176 patients were in the experimental group. Five patients were excluded from the control group because of transfer of medical care to another provider. Six patients were excluded from the experimental group and seven patients were excluded from the control group because of incomplete addresses.

Attendance rates then were determined for the control (n = 147) and experimental groups (n = 170), for new and return patients, and for both the 1- to 4- and 1- to 8-week time windows (measured from the date of the original failed appointment). Many of the rescheduled patients attended at times other than their rescheduled clinic date. However, in order to be counted as attending, they had only to attend within the studied time window. All comparisons then were analyzed by use of χ^2 tests or z tests.

The economic status was compared for patients with rescheduled failed and regular appointments. Also, we analyzed the attendance rates of rescheduled failed appointments for return patients in the experimental group to determine if the number of times a patient had failed an appointment and was rescheduled had an effect on attendance.

RESULTS

The efficacy of recalling patients who failed their appointments by computer generated postcard prompters is shown in Table 2. This intervention resulted in a 21% increase in attendance of new patients and a 30% increase of return patients compared to controls. There were two new patients in the experimental group who canceled their rescheduled appointments and attended just after the 4-week time window. These patients were counted as failed in the analysis. Rescheduling patients 6 to 7 weeks as compared to 2 to 3 weeks after the failed appointment did not cause a statistically significant difference in patient attendance (Table 3). However, there was a trend toward better attendance in the return patients who were rescheduled in the 2- to 3-week time period.

TABLE 3. ATTENDANCE RATES WITH USE OF POSTCARD RESCHEDULING TECHNIQUE FOR 8-WEEK FOLLOW-UP

	No. of Patients		
	New	*Return*	*Total*
Control*			
Attended	19	39	58
Failed	38	51	89
Total	57	90	147
Experimental†			
Attended	21	55	76
Failed	41	53	94
Total	62	108	170
χ^2	p<.951	p<.287	p<.345

*Appointment was rescheduled for sixth or seventh week.

†Appointment was rescheduled for second or third week.

Many patients failed several different new and return appointments over the course of the study. All of these failed appointments were rescheduled. The possibility exists that the repeated rescheduling of patients selected a group of individuals who were more responsive to this rescheduling technique. Table 4 shows attendance as a function of the number of times a patient had been rescheduled. It can be seen that there was no statistically significant difference between patients rescheduled once or twice and that there was a nonsignificant tendency toward reduced attendance for patients rescheduled three or more times. Thus, patient selection was not responsible for the efficacy of this technique in return patients.

Another concern is that this technique might be effective only for higher-income patients and that it does not recapture patients with a lower socioeconomic background. Table 5 shows the average income of patients, in all subject groups, who attended regular and rescheduled failed appointments. Income for patients from the rescheduled failed appointment group was only 62% of that for patients attending regular appointments. This difference is actually greater than it appears, because recalled patients are returned to regular follow-up, and will thus lower the average income of the regular appointment group. The system is, thus, effective. However, in clinics that have a borderline financial status, lowering the private-pay-to-indigent patient ratio may not be economically desirable.

TABLE 4. EFFECT OF REPEATED RESCHEDULING OF RETURN PATIENTS IN EXPERIMENTAL GROUP

	No. of Patients	*Attendance Rate*
Rescheduled once	59	49%
Rescheduled twice	31	52%
Rescheduled three or more times	18	33%

*By z test, none of rates were significantly different from each other.

TABLE 5. AVERAGE INCOME AND POVERTY LEVEL OF PATIENTS WHO ATTENDED RESCHEDULED FAILED APPOINTMENTS COMPARED TO REGULAR APPOINTMENTS

	Regular Appointments	*Rescheduled Appointments*
Average yearly income	$10,082	$6,300
Standard deviation	$11,005	$5,600
Number	843	88
Unpaired *t* test	$p < .002$	
Poverty level*	13.30%	−58.37%
Standard deviation	226.56%	121.72%
Number	843	88
Unpaired *t* test	$p < .004$	

All patient groups are included. Data were obtained by questionnaire during patient's medical appointment and/or home visits. Not all families would volunteer their income, so data are not available on all patients.

*Zero percent is equal to poverty level, defined as $5,000/yr for single-member family and raised by $1,250 for each family member over one.

DISCUSSION

In order to recapture patients who do not attend their medical visits, the patient must be contacted and an attempt at appointment rescheduling made. This contact may be made by mail, phone, or home visit; and initiated either by the agency referring the patient or by that providing the health care. Also, nonaffiliated social service resources may be involved in this process.

The Delta Project's computer system will reschedule automatically all new and return patients who have failed their appointments and contact these patients by postcard. This method has been found to be both effective and cost-efficient. Twenty-one percent of new patients (above control levels) and 30% of return patients (above control levels) attended appointments following this process. The overall cost of recapturing a new patient was $3.00, and a return patient, $2.00. This operational cost does not include a $2,500 start-up investment for hardware (Macintosh Plus, hard disk drive, and run-time version of Omni 3+). If the system is used for billing, then only a portion of the start-up cost needs to be applied to the patient tracking activities. The technique was most effective in recalling return patients the first and second times they failed an appointment (Tables 2 and 4). The economic status of patients who attended rescheduled appointments was significantly lower than that of patients attending regular appointments (Table 5). Thus, the system is effective in reaching its target population. However, in clinics that have a borderline financial status, lowering the private-pay-to-indigent patient ratio may not be economically feasible. It would be expected that a lower ratio will result in a decrease in revenue collection regardless of the fee structure used in patient billing.

Four methods have been used to reschedule patients who have failed their appointments: letters, postcards, phone calls, and, to a lesser extent, home visits. In our protocol we used postcards and home visits. A letter, although more informative, may be also more confrontational and is more costly for the clinic to generate. Using postcard prompters, Hulka[19] rescheduled failed appointments of new patients for cervical cancer screening. She found that 28.7% of the patients could be made to attend appointments by the first rescheduling attempt, and only 7.9% by a second (no controls). The success reported in this study is comparable with our reported new patient attendance of 31% (Table 2).

Home visits also were found to be effective, even though these visits occurred months after the appointment, and on a group of patients who did not attend appointments after repeated prompting by postcards. Twenty-three percent of those contacted eventually called for an appointment and attended a follow-up visit. The cost of each home visit was $24. If one assumes that patients are only home in approximately 50% of the home visits attempted (35% in our patients and 37% of those of Banco and Segarra[20]), and if one assumes 50% of the contacts result in an attended medical appointment, the cost of home visits per recovered patient approaches $100. This demonstrates the economic problem of solely using primary case management and social service techniques in this population, and also illustrates the need for triaging of the available social service resources to families that need them the most.

Another technique used by the patient management system to recoup patients who had failed their appointments was the automatic notification of the referring health care professional regarding the patient's appointment attendance or lack thereof (along with a brief summary of the medical findings and treatment plan). We found this technique to be useful not only in promoting patient medical compliance, but also in forming linkages between our agency and the referring physician. Referring physicians often assume that patients who failed to attend their appointments actually were seen and the medical findings were not sent to them.

Finally, attendance ratios were automatically calculated for all patients. Patients whose ratios were low had their medical records reviewed. When repeated contacting of these families did not bring satisfactory results and the illness was felt to be potentially threatening to the child, the family was referred to the Department of Human Services for further intervention.

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THE INTERNATIONAL SYMPOSIUM ON CLINICAL AND BASIC OTOLOGY

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COMPARATIVE HISTOLOGY OF THE TYMPANIC MEMBRANE AND ITS RELATIONSHIP TO CHOLESTEATOMA

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The purpose of this study was to determine whether anatomic differences in the tympanic membranes of various species could explain differences in the propensity to form aural cholesteatomas and retraction pockets. Tympanic membranes from humans, dogs, cats, rabbits, guinea pigs, rats, gerbils, and mice were examined histologically. The pars flaccida and pars tensa varied greatly among the species studied. The guinea pig's pars flaccida was very small and had a thin lamina propria. In contrast, the lamina propria of the rabbit and cat pars flaccida were thick. The amount of collagen, elastin, mast cells, and macrophages varied widely. The human and gerbilline tympanic membranes were anatomically dissimilar; for example, the human pars flaccida and pars tensa contained more and denser collagen than did those of the gerbil. The presence of macrophages or mast cells did not correlate with the propensity to develop cholesteatomas. Therefore, anatomic differences among these species do not explain why some develop aural cholesteatomas and others do not.

KEY WORDS — cholesteatoma, otitis media, tympanic membrane.

INTRODUCTION

When the human tympanic membrane is subjected to constant inward pressure, retraction with or without cholesteatoma formation may occur. Eustachian tube obstruction may result in retraction pockets of the pars flaccida or pars tensa; blockage of the external auditory canal by trauma or keratin accumulation (keratosis obturans) may result in cholesteatoma with invasion of the middle ear. Similarly, Mongolian gerbils develop retraction pocket cholesteatomas[1] after eustachian tube cautery, and gerbils and rabbits develop ear canal cholesteatomas after ear canal blockage.[2,3] Several other mammals do not develop retraction pockets or cholesteatomas under similar conditions. Dogs,[4,5] cats,[6] and rats[4,7] do not develop retraction pockets after eustachian tube obstruction, and cats, guinea pigs, rats, hamsters, and mice do not develop canal cholesteatomas after ear canal ligation.[8]

The purpose of this study was to compare the histology of the tympanic membrane of nine different mammalian species to identify anatomic features that might explain why certain species develop retraction pockets and cholesteatomas and others do not.

MATERIALS AND METHODS

Tympanic membranes from the following animals were obtained and fixed in situ: mouse, rat, hamster, gerbil, guinea pig, rabbit, cat, and dog. Human tympanic membranes were obtained at autopsy from individuals with no history of ear disease. Three or four animals of each species were examined. Each specimen was fixed in 2% paraformaldehyde, 2% glutaraldehyde in 0.08 mol/L cacodylate buffer for at least 4 hours at 4°C. Specimens were dehydrated in graded acetone solutions, embedded in Epon-araldite, and sectioned 1 μm thick with glass knives. The plane of sectioning was perpendicular to the pars flaccida and parallel with the long process of the malleus. Sections were stained with toluidine blue/basic fuchsin or with an elastin stain (orange G, aniline blue, and acid fuchsin). Each tympanic membrane then was studied for the presence and quantity of collagen, elastin, keratin, mast cells, and macrophages. Gerbil aorta was used as a control for the elastin stain.

Each pars flaccida and pars tensa were examined and graded for the presence of collagen, elastin, mast cells, macrophages, and keratinization. An arbitrary scale of 0 to + + + + was used to demonstrate differences between species. Not all specimens from a species were the same; average values are given (Table 1).

RESULTS

The gross appearance and size of the tympanic membrane varied less than the overall size of the animals studied (Fig 1). The pars flaccida and pars tensa varied greatly among the species studied (Figs 2-4).

In each of the species studied, the pars flaccida tended to be thicker than the pars tensa; it contained less collagen and more mast cells and was keratinized more heavily. The presence of keratin lamellae in each specimen was variable. The human tympanic membrane had a distinct pars flaccida and pars tensa (Fig 2). The pars tensa con-

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TABLE 1. PRESENCE OF VARIOUS SUBSTANCES IN TYMPANIC MEMBRANES

	Collagen	*Elastin*	*Mast Cells*	*Macrophages*	*Keratin*
Human					
Pars flaccida	+ + + +	+ +	+	0	+ +
Pars tensa	+ + + +	+ +	+	0	+ +
Dog					
Pars flaccida	+ + +	+	+	+	+ + +
Pars tensa	+ + + +	+	0	0	+ +
Cat					
Pars flaccida	+ +	0	+	0	+ + +
Pars tensa	+ + + +	0	+	+	+ +
Rabbit					
Pars flaccida	+ +	+	+	+ +	+
Pars tensa	+ + + +	+	+	+	+
Guinea pig					
Pars flaccida	+	0	+ +	0	+
Pars tensa	+ + + +	0	0	0	+
Rat					
Pars flaccida	+	0	+	+	+ +
Pars tensa	+ + + +	0	0	0	+
Hamster					
Pars flaccida	+ + +	+ +	+	+	+ +
Pars tensa	+ + + +	+	0	0	+ +
Gerbil					
Pars flaccida	+	+	+ +	+	+ +
Pars tensa	+ + +	+ +	0	0	+
Mouse					
Pars flaccida	+	0	+	0	+ +
Pars tensa	+ + +	+	0	0	+

Arbitrary scale indicates relative amounts.

tained thick, tightly packed collagen bundles, while the pars flaccida contained more irregular and more loosely packed collagen bundles. The human tympanic membrane was keratinized uniformly over the pars flaccida and pars tensa. Mast cells were seen in the pars flaccida, but not the pars tensa (Fig 4D); elastin fibers were identified throughout the human tympanic membrane (elastin stains not illustrated; Table 1).

The tympanic membranes of the human, dog, cat, rabbit, hamster, rat, and mouse were similar in that they had a thin, dense pars tensa and a thick pars flaccida with loosely oriented collagen fibers (Figs 3A-C and 4B-D). In contrast, the pars flaccida of the gerbil appeared more cellular than the others examined (Fig 4A). The pars flaccida of the guinea pig was much smaller than that of the other species examined (Fig 3D).

The guinea pig pars flaccida was not grossly evident, but could be distinguished on histologic sections (Fig 3D). The pars flaccida of the guinea pig was no thicker than the pars tensa, but the collagen fibers were sparse compared to those of the pars tensa.

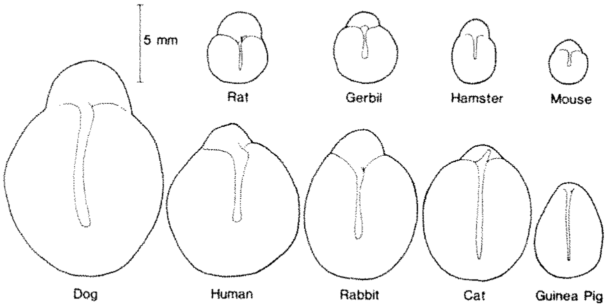

Fig 1. Diagrams of tympanic membranes from species studied, showing relative sizes and shapes.

Mast cells within the pars flaccida were present in each of the species studied. Only the human, cat, and rabbit pars tensa contained mast cells. Macrophages were seen in most species (Fig 4A and Table 1).

DISCUSSION

The human tympanic membrane may respond to chronic inward force by medial displacement. This inward force may be due to negative middle ear pressure from eustachian tube blockage or positive external ear pressure due to keratin accumulation. In some cases this medially directed pressure leads to retraction pockets of the tympanic membrane, and at times, cholesteatoma. Inflammation may be necessary for these events to occur. Similarly, ger-

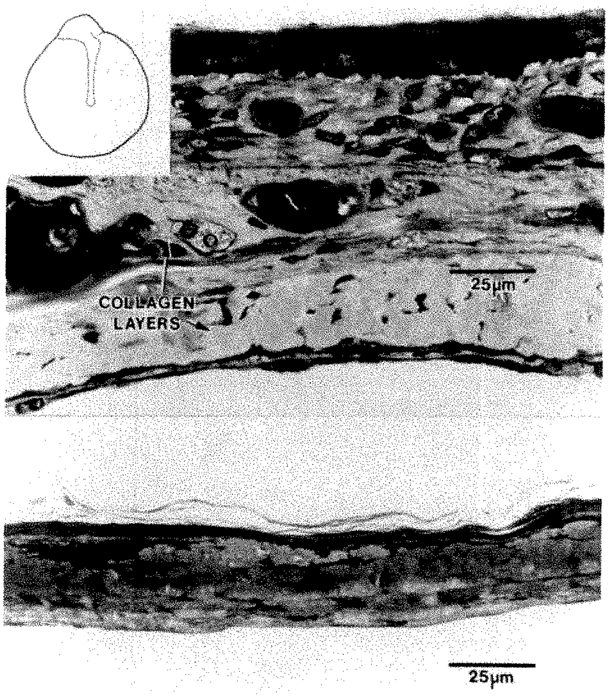

Fig 2. Histologic sections of human tympanic membrane (toluidine blue and basic fuchsin). Upper — pars flaccida, lower — pars tensa, inset — diagram of whole tympanic membrane.

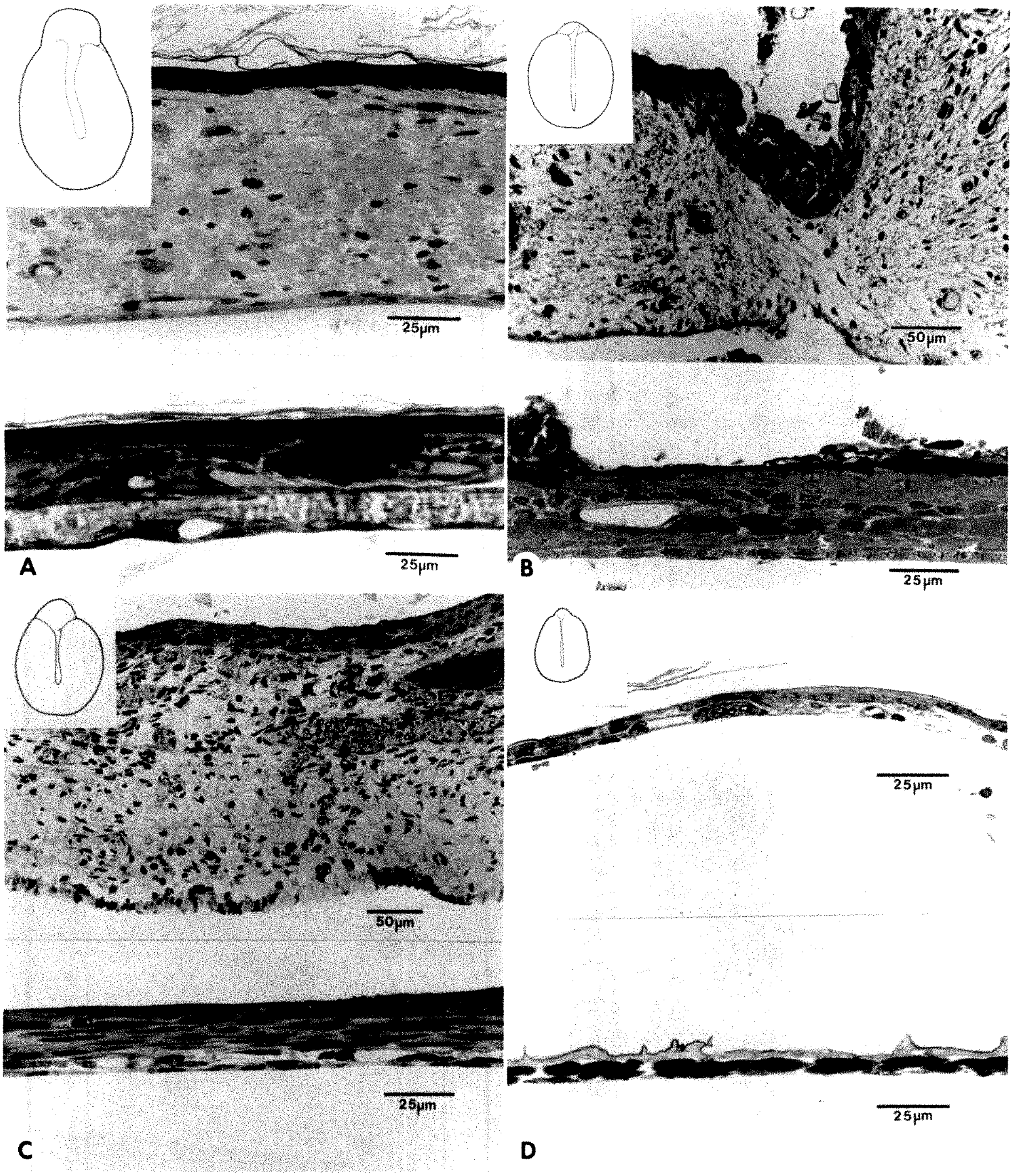

Fig 3. Histologic sections of tympanic membranes (toluidine blue and basic fuchsin). Upper — pars flaccida, lower — pars tensa, inset — diagram of whole tympanic membrane. A) Dog. B) Cat. C) Rabbit. D) Guinea pig.

bil[1,2] and rabbit[3,9] tympanic membranes become displaced medially and form cholesteatomas by the same mechanism. No anatomic similarities among the human, gerbilline, and rabbit tympanic membranes could be identified that would explain why these ears respond differently from those of other species studied (Table 2[1,2,4-9]).

The anatomic features of the tympanic membranes of studied animals were similar to those previously described. The tympanic membrane of the dog was the largest in this group of mammals and was as previously described.[10,11] The tympanic membrane of the dog does not form retraction pockets or cholesteatomas with eustachian tube obstruction.[4,5] The effects of ear canal ligation in dogs are unknown.

Similarly, the cat's tympanic membrane does not form retraction pockets after eustachian tube block-

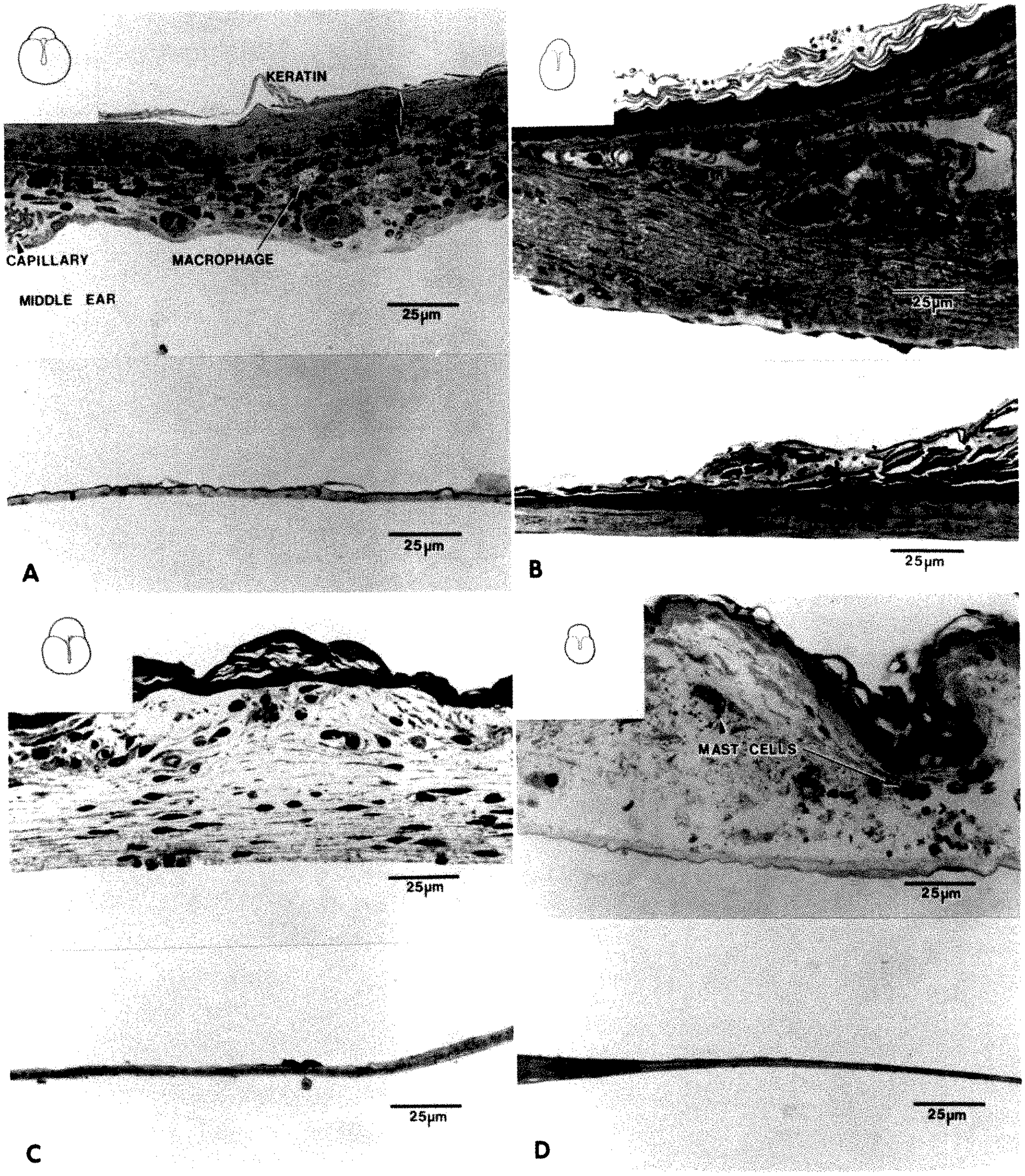

Fig 4. Histologic sections of tympanic membrane (toluidine blue and basic fuchsin). Upper — pars flaccida, lower — pars tensa, inset — diagram of whole tympanic membrane. A) Gerbil. Double-headed arrow — keratinizing squamous epithelium. B) Hamster. C) Rat. D) Mouse.

age, or cholesteatomas after ear canal blockage.[8] The tympanic membrane of the cat has been well described, and previous descriptions are consistent with the findings in our study.[12,13]

The tympanic membrane of the rabbit has a distinct but small pars flaccida that is three to five times as thick as the pars tensa and has frequent mast cells and macrophages. Steinbach[3] and Steinbach and Grüninger[9] suggested that "irritants" and "non-irritants," including ear canal ligation, applied to the rabbit tympanic membrane induced cholesteatomas. The pars flaccida of the rabbit appeared similar to those of the cat, rat, gerbil, and mouse (Figs 1-4).

The tympanic membrane of the guinea pig had an extremely small pars flaccida that was best seen on histologic section (Fig 3D). This finding is consistent with those of other investigators,[12,13] al-

TABLE 2. RESPONSE OF EARS TO EUSTACHIAN TUBE OBSTRUCTION OR EAR CANAL LIGATION

	Severe Retraction From Eustachian Tube Obstruction	*Cholesteatoma From Ear Canal Ligation*
Human*	Yes	Yes
Dog	No[4,5]	ND
Cat	No[6]	No[8]
Rabbit	ND	Yes[9]
Guinea pig	ND	No[8]
Rat	No[7]	No[8]
Hamster	ND	No[8]
Gerbil	Yes[1]	Yes[2,8]
Mouse	ND	No[8]

ND — no data available.

*Clinical observations have shown severe retraction pockets and cholesteatoma due to eustachian tube obstruction; likewise, ear canal obstruction may result in ear canal cholesteatoma.

though some have suggested that the guinea pig has no pars flaccida.

The tympanic membrane of the gerbil[14,15] had a well-defined pars flaccida and pars tensa. The pars flaccida has been referred to as an "accessory tympanic membrane,"[14] but there is no bony separation of the pars flaccida from the pars tensa. Thus there is little justification for the use of the term "accessory tympanic membrane" in the Mongolian gerbil.

The tympanic membrane of the hamster (Fig 4B) had a distinct pars flaccida and pars tensa. Both portions of the tympanic membrane were keratinized heavily. The pars flaccida, as in most other rodents studied, was thicker than the pars tensa. However, the pars flaccida of the hamster contained dense collagen bundles without the extracellular spaces seen in the gerbil, rat, and mouse. The hamster tympanic membrane does not become medially displaced with ear canal blockage.[8]

The rat and mouse tympanic membranes were similar (Fig 4C,D). They have a pars flaccida with a large lamina propria with small, irregularly arranged collagen fibers. The anatomy of the rat[16] and mouse[17] tympanic membranes was consistent with previous descriptions.

Mast cells were present in the pars flaccida of each of the animals studied (Table 1), as well as in the human, cat, and rabbit pars tensa. The consistent appearance of mast cells in each of these species gives credence to their importance, as ascribed by several investigators.[16,18,19]

Histochemical studies for elastin failed to identify elastin fibers in the pars flaccida of the cat, guinea pig, rat, and mouse and in the pars tensa of the cat, guinea pig, and rat. The role of elastin fibers within the tympanic membrane is unknown. Our findings are consistent with those of Nishiyama[20] and Lim[21] in the human and corroborate Shrapnell's original observations.[22] The presence or absence of elastin staining fibers in the tympanic membrane did not correlate with the propensity of the tympanic membrane in some species to form retraction pockets and cholesteatomas.

The propensity of the tympanic membrane of some species to form retraction pockets and cholesteatomas does not seem to be associated with any particular characteristic. The tympanic membranes of the three animals known to develop retraction pockets and cholesteatomas are morphologically dissimilar, having different concentrations of elastin and collagen. Furthermore, morphologic characteristics that have been thought of as important in the development of cholesteatomas, such as elastin, are present in some non–cholesteatoma-forming animals (Table 2[1,2,4-9]).

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THE DEAFNESS RESEARCH FOUNDATION OTOLOGICAL RESEARCH FELLOWSHIP FOR THIRD YEAR MEDICAL STUDENTS

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AIR CONDUCTION THRESHOLDS AND SECRETORY OTITIS MEDIA: A CONVENTIONAL AND EXTRA-HIGH FREQUENCY AUDIOMETRIC COMPARISON

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A comparison has been made of air conduction threshold changes up to 1 year after myringotomy, aspiration of middle ear fluid, and insertion of ventilation tubes in ten patients with bilateral and 12 with unilateral secretory otitis media (SOM). Pure tone air conduction thresholds have been analyzed in three frequency groups: low frequency (LF; 0.25, 0.5, and 1 kHz), high frequency (HF; 2, 4, and 8 kHz), and extra-high frequency (EHF; 10, 12, 14, and 16 kHz). In the LF and HF ranges, significant improvement came during the first 24 hours after intubation, while in the EHF range, threshold lowering occurred gradually over the following 2 months. Possible explanations for these findings are discussed.

KEY WORDS — high frequency audiometry, middle ear transmission, secretory otitis media, tube placement.

INTRODUCTION

Secretory otitis media (SOM) is characterized by the presence of nonsuppurative effusion in the middle ear cleft and is the most common cause of hearing loss in children.[1] It usually affects both ears and has been seen more frequently in the past two or three decades, although this trend can be ascribed to more efficient diagnosis.[2]

Adenoidectomy, myringotomy with aspiration of middle ear fluid, and transmyringeal insertion of ventilation tubes are widely used surgical methods of treatment. Institution of treatment is recommended only after an observation period of at least some weeks or months, on account of the marked tendency to spontaneous improvement.[1,3]

By far the most common clinical feature is hearing loss, which may vary from negligible to 50 to 60 dB, with a mean of 28 dB.[4,5] Air conduction thresholds of 15 to 25 dB hearing level or better have been reported after observation periods of 3 to 8 years in 76% to 95% of ears with chronic SOM treated by ventilation tubes,[3,6] but no studies have described the immediate and short-term effects of this treatment.

In the studies cited above, pure tone audiometric evaluation has been restricted to the conventional frequencies from 0.125 to 8 kHz. Interest in extra-high frequency (EHF) audiometry with determination of air conduction thresholds in the frequency range of 8 to 20 kHz has become more widespread since the 1960s.[7-9] Interlaboratory comparisons were impossible earlier because custom-built instruments were employed, but the introduction of a commercial EHF audiometer[10] has remedied this situation and has permitted the establishment of normative data.[8]

The aim of this study was to investigate prospectively the changes over time in air conduction thresholds in both the conventional and EHF audiometric ranges following myringotomy and insertion of ventilation tubes.

MATERIAL AND METHODS

The study group consisted of ten patients with bilateral and 12 with unilateral SOM, for a total of 32 ears. Six of the patients with unilateral SOM had quiescent otopathology and/or slightly elevated conventional audiometric thresholds in the opposite ear. Myringotomy and insertion of a ventilation tube in the posteroinferior quadrant was performed in 1986 or early 1987 after an observation period of 3 to 6 months. Sixty-four percent of the patients were male and 36% were female. The median age at operation was 13 years (range, 7 to 28 years). Mean observation time after operation was 6½ months (range, 3 weeks to 12 months).

Conventional air and bone conduction audiometry was performed the day before or the actual day of operation, together with determination of air conduction thresholds in the EHF range of 8 to 20 kHz. Conventional and EHF audiometry was repeated immediately after or within 24 hours of tube placement and subsequently at different intervals up to 1 year postoperatively. The instruments employed for conventional and EHF audiometry were the Madsen OB822 and the Demlar 20K audiometers, respectively. Threshold measurements were performed in a sound-insulated room that satisfied

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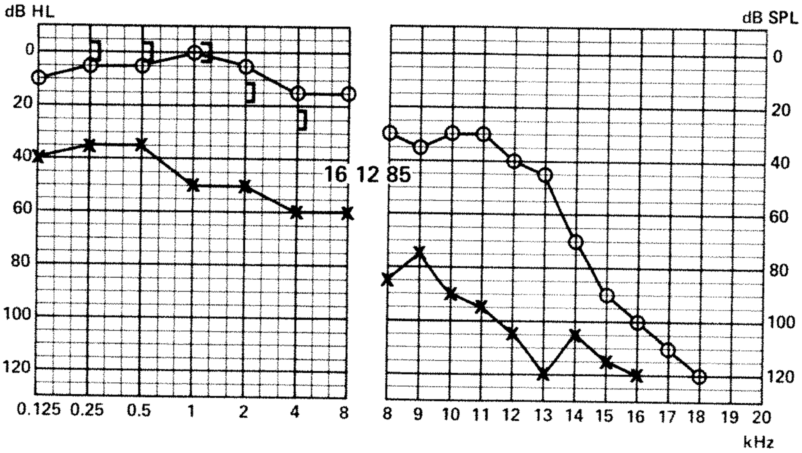

Fig 1. Preintubation conventional (dB hearing level) and extra-high frequency (dB sound pressure level) thresholds in patient with unilateral secretory otitis media. Note linear frequency scale above 8 kHz.

ISO/DIS 8253 requirements.[11] Audiometer calibration was performed at regular intervals.

The postoperative air conduction thresholds for each patient were subtracted from the corresponding preoperative measurements. This was done at octave intervals from 0.125 to 8 kHz in the conventional audiogram, and at 2-kHz intervals from 10 to 16 kHz for the EHF thresholds. Occasionally, an EHF threshold was not recordable before surgery, even at maximum output (120 dB sound pressure level), for frequencies at which a postoperative threshold could be obtained. In these few cases, no comparison was made between preoperative and postoperative thresholds. Three groups have been compared: low frequency (LF; 0.25, 0.5, and 1 kHz), high frequency (HF; 2, 4, and 8 kHz), and EHF (10, 12, 14, and 16 kHz). The means and standard deviations of the differences between the preoperative and postoperative air conduction thresholds were calculated for each frequency and for grouped frequencies.

Threshold changes also were studied as a function of time during the postoperative observation period. Significance estimations were made with Student's *t* test.

RESULTS

In Fig 1 is shown the preoperative audiogram of one of the patients with unilateral SOM; air conduction threshold in the SOM ear was 30 to 50 dB higher in the conventional audiometric range and up to 75 dB in the EHFs. The immediate postintubation thresholds and the results 3 months later are presented in Fig 2. Closure of the air-bone gap occurred in the frequency range up to and including 2 kHz immediately after operation, while the EHF threshold was unchanged at this time, but was identical to that of the contralateral, normal ear 3 months later. This delayed threshold improvement in the EHF range was a consistent feature in all SOM ears, the period required for threshold normalization varying from 2 to 8 weeks. Within the first 24 hours, 95%, 84%, and 43% of the final threshold improvement occurred in the LF, HF, and EHF ranges, respectively.

The mean and standard deviation of both the immediate and final air conduction changes for all frequencies are shown in Fig 3. The improvement within the first 24 hours after intubation is highly significant in the LF and HF ranges ($p<.005$), whereas this is not the case in the EHF range ($p>.05$). The EHF threshold improvement became significant at 2 months ($p<.05$), and no significant changes in threshold occurred after this time in any of the three frequency ranges.

It is of interest to know whether the final hearing thresholds measured in this series represent a normalization. In only six cases were we able to com-

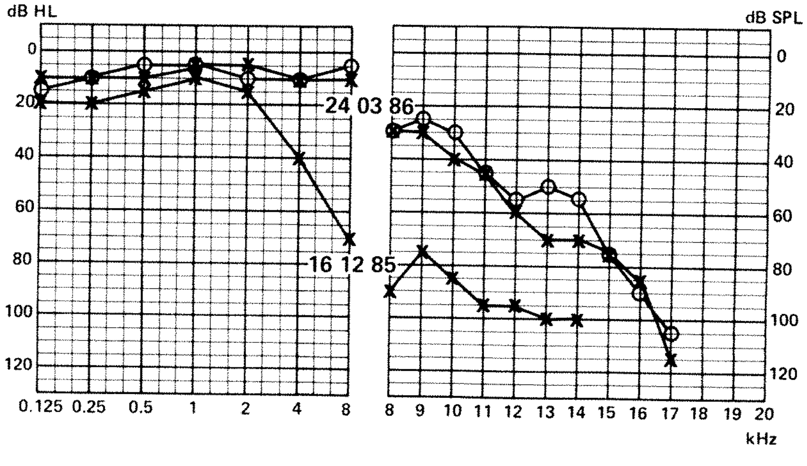

Fig 2. Air conduction thresholds immediately after intubation of left ear (Dec 16, 1985) and 3 months later (March 24, 1986). Threshold normalization occurred up to and including 2 kHz on day of operation, while threshold is virtually unchanged in 8- to 14-kHz range. High frequency and extra-high frequency thresholds are, however, symmetric 3 months later.

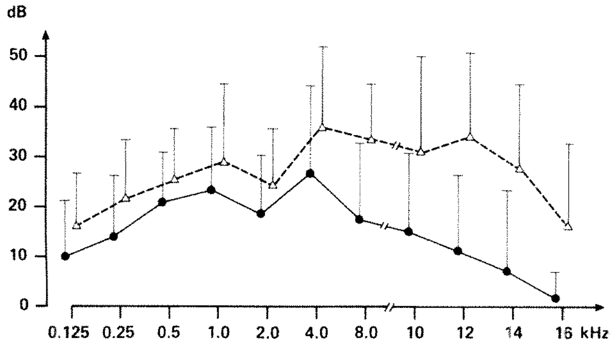

Fig 3. Immediate (●—●) and final (△---△) air conduction threshold improvement (mean + SD) for all frequencies recorded following intubation, showing delayed threshold improvement in extra-high frequencies and, to lesser extent, in high frequencies.

pare hearing threshold development in a grommet-treated ear with a healthy ear in the same patient. In each case, in the conventional range the final pure tone threshold was a complete normalization compared to the healthy ear, while in the EHF range this was the result in only two ears. The mean final EHF difference between the six healthy and the six treated ears was 16 dB.

DISCUSSION

The complete conventional and EHF ranges contain six and one octaves, respectively. The former was, therefore, subdivided into LF and HF ranges in order to reduce this discrepancy to some extent.

The main finding in the present study is that intubation produces an immediate and statistically significant improvement of air conduction thresholds at the conventional audiometric frequencies, especially in the LF range, whereas improvement is significantly delayed in the EHF range. Only after several weeks does EHF hearing improvement reach statistically significant levels. The final threshold improvement is, however, nearly identical in the three frequency ranges.

An explanation for these results is difficult to find in light of the present state of knowledge of middle ear transmission at EHFs. The following factors may, however, be relevant. By a combination of pressure amplification and lever action, the middle ear acts as an impedance transformer to optimize the flow of acoustic energy from air to the fluids of the inner ear. As far as these processes of the middle ear are concerned, the concept of mechanical resonance is fundamental.[12] In such a mechanical system two reactive elements, mass and stiffness, interact. When the reactances of these are equal and opposite, they cancel each other out and a resonance occurs. At frequencies below resonance, the response is determined by the stiffness of the system, and at frequencies above resonance, by the mass. The middle ear ossicles have mass, and stiffness is provided, inter alia, by the supporting ligaments and the tympanic membrane. The resonance of this system occurs at about 0.8 to 1.2 kHz in humans.[12]

It is a common clinical experience that aspiration of the middle ear after myringotomy is frequently incomplete, and that viscid secretion retracts upward toward the epitympanum. Sadé et al[13] have shown that middle ear ventilation and clearance of mucus in intubated ears is independent of whether or not mucus aspiration has been performed. Hearing improvement, in the conventional frequency range, was also identical in the two groups. The criterion of clearance in their study was otomicroscopic observation through the ventilation tube, which permits only a very restricted inspection of the middle ear mucosa. That this is an inadequate method of assessment is confirmed by the recent report that the middle ear space continues to increase in volume up to 3 months after intubation.[14] This finding supports the view that retention of secretion and/or mucosal edema may persist for a considerable period after the middle ear cleft has been ventilated.

Ventilation of the mesotympanum may reduce the stiffness of the middle ear transformer sufficiently to allow threshold normalization at the conventional audiometric frequencies, whereas lesser amounts of retained mucus or mucosal edema in the epitympanum or in the window niches may either increase the mass of the system, and thus delay threshold improvement in the EHF range, or influence the incudomalleal rotation axis, which is known to be frequency dependent.[15] Subsequent resorption of epitympanal mucus, or its removal by mucociliary transport, could then be reflected in a gradual lowering of EHF thresholds, as demonstrated in this study. Residual epitympanic or circumossicular disease could result in a permanent increase in the mass of the system and thus persistently high EHF thresholds, as was observed in four of our six patients with unilateral SOM.

Additional factors are the presence of a defect in the tympanic membrane after intubation and the presence of the ventilation tube, which has an appreciable length relative to the thickness of the drumhead. The effect of the grommet will be variable, since resistance of a canal is related directly to length. The vibration pattern of the tympanic membrane becomes exceedingly complex at higher frequencies,[16] and decoupling of the membrane from the mallear handle occurs at frequencies above 3 to 4 kHz in both cats and humans.[17,18] Unfortunately, the EHF range has not been investigated in any of the cited studies, and the eventual contribution of these factors to transmission at these frequencies is at present speculative.

Indeed, it could be argued that the ossicular chain does not contribute appreciably to transfer of EHF acoustic energy to the inner ear — this possibility could also explain the high thresholds at these frequencies — and that stapes footplate movements are a result of direct acoustic stimulation from the tympanic membrane. The pathologic epitympanic changes postulated above could, however, influence stapes movements as a result of changes in reactance.

This investigation has employed only air conduction audiometers, and it therefore is not possible to exclude inner ear damage as an explanation, possibly partial, of the higher thresholds in the EHF range. The inability to differentiate between middle and inner ear disease was also the case in the study of Mair and Laukli[9] comparing air conduction thresholds after myringoplasty and stapes surgery for otosclerosis in both the conventional and EHF ranges. That study revealed significant threshold loss in the EHF range following both procedures, and the conclusion was drawn that EHF audiometry may have value as a sensitive monitor of middle ear surgical techniques. That simple otosurgical procedures can result in excessive pressure changes in the inner ear has been illustrated by the report of sensory hearing loss due to round window fistulas, which were confirmed at tympanotomy, following "traumatic" myringotomies in two patients.[19] This must, however, be a very rare event. Cochlear mechanics will ensure that the basal portion of the basilar membrane will be most vulnerable to such pressure fluctuations.

The proximity of the basal cochlear duct to the round window also renders the EHF region more vulnerable to damage from the spread of infection or toxins from the middle ear through the round window membrane.[20] A temporary elevation of bone conduction thresholds in the conventional audiometric range during the course of both purulent otitis media and SOM has been described by several authors,[21,22] although others have reported that bone conduction thresholds are not affected.[5] Permanent elevation of bone conduction thresholds, increasing successively from 0.5 to 4 kHz, has been documented in 20% of cases of SOM, particularly those of long duration.[23] Permanent damage to the basal cochlear duct has been postulated to occur as a result of leakage of toxins from the middle ear through the round window membrane and/or a local hypoxia,[23] since perilymphatic oxygen tension in the basal coil is partly dependent on gas diffusion from a ventilated tympanic cavity.[24]

There is only one other report in the literature in which EHF air conduction thresholds have been studied in SOM[25]; permanent elevation of EHF thresholds was found in a few cases, and this was greatest in those ears that had presented with the largest pretreatment air-bone gaps in the conventional audiometric range.

Further studies are necessary to elucidate the relative contributions of middle and inner ear disease in the EHF range. The recent introduction of the electric transduction audiometer[26] and of a new bone vibrator,[27] both of which permit audiometric assessment of inner ear function up to around 16 kHz, should provide clarification.

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EXTERNAL AND MIDDLE EAR MALFORMATIONS: AUTOSOMAL DOMINANT GENETIC TRANSMISSION

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Congenital malformations of the external and middle ear are relatively frequent anomalies (one to five cases in 20,000 live births). They are part of genetic syndromes such as Treacher Collins and Goldenhar's syndromes, but most cases are isolated and sporadic. A few cases of familial incidence of isolated external and middle ear malformations with autosomal recessive, autosomal dominant, and sex-linked modes of transmission have been described. We report on two siblings with almost identical anomalies of the external and middle ear and no other congenital defects. Their father had similar malformations, but nobody else in his large sibship presented ear malformations. The defects were also absent in two previous generations. We discuss the possibility, not previously mentioned in the literature, that these congenital malformations could have appeared by spontaneous mutation in the father and transmitted themselves as an autosomal dominant trait to his children.

KEY WORDS — external and middle ear, genetic transmission, malformations.

INTRODUCTION

Congenital malformations of the external and middle ear are part of genetic syndromes involving structures derived from the first and second branchial arches (Treacher Collins syndrome, Goldenhar's syndrome).[1] They also present as a component of syndromes associated with chromosomal aberrations (Turner's syndrome).[2]

When appearing as the only congenital anomalies, most cases of external and middle ear malformations are believed to be sporadic.[1] However, a few cases have been described in the literature that seem to be transmitted genetically.[1,3-8] In some instances the mode of transmission is most likely autosomal recessive,[1,3,5] while others display an autosomal dominant pattern of transmission.[7,8] There is one family described in which a sex-linked pattern of genetic transmission was encountered.[2]

In this report we describe two siblings with almost identical external and middle ear malformations not associated with other congenital defects. Their father had similar anomalies, but nobody else in his family had ear malformations. Their mother and her family were normal, and there was no consanguinity between father and mother. The anomalies that were present in the middle and external ear were documented during microsurgical reconstructive procedures and have not been associated before with heredity.

CASE REPORTS

Case 1. A 7-year-old boy presented with hearing loss and difficulty in acquiring normal language. At physical examination we noticed microtia type II in the right ear and type I in the left ear (Fig 1A). The external ear canals were stenotic, but the tympanic membranes were present on both sides. There was a partial facial paralysis on the right side involving the ramus mandibularis. According to the grandmother, this had always been present. There were no other anomalies at physical examination. An audiogram on April 2, 1986, showed a 60-dB air-bone gap bilaterally (Fig 1B) and normal speech discrimination. Mastoid x-ray films showed a well-pneumatized mastoid and middle ear with a normal-appearing ossicular chain bilaterally. On June 26, 1986, the boy was taken to the operating room, and a right exploratory tympanotomy was performed through a postauricular incision with general anesthesia. After developing the tympanomeatal flap, we enlarged the stenotic canal with a bur to allow easy access to the middle ear. There was a deformed malleus and incus (Fig 2A, middle) that were fixed in the attic. There was no stapes superstructure, and the oval window was closed solidly by bone (Fig 2B). A slight groove in the bone suggested the contour of the oval window, but there was no annular ligament. The facial nerve was in its normal position and covered by bone. The round window was normal. We fenestrated the oval window and used the deformed malleus-incus as a columella from the window to the tympanic membrane (Fig 2C). On Oct 6, 1986, an audiogram (Fig 1C) showed a 30-dB hearing improvement across the speech frequencies.

Case 2. The 10-year-old sister of the patient described above came to us because of hearing loss and language difficulties that were present since birth, according to the grandmother. During the last 6

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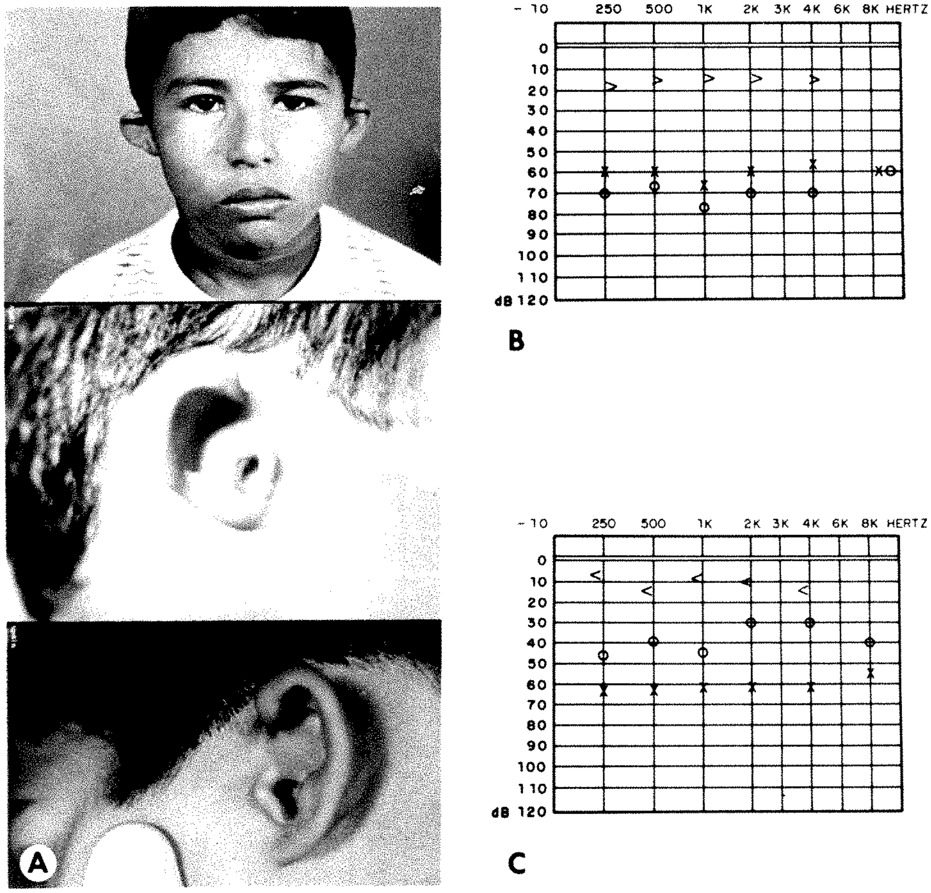

Fig 1. (Case 1) A) Bilateral microtia and partial facial paralysis on right side (top), microtia type II and stenotic external auditory canal in right ear (middle), and microtia type I and stenotic external auditory canal in left ear (bottom). B) Preoperative audiogram. C) Postoperative audiogram.

years she had had intermittent otorrhea from the right ear. Physical examination showed type I microtia on both sides (Fig 3A). The external ear canals were stenotic, and there was a central perforation of the tympanic membrane on the right side. Audiometry showed a bilateral 60-dB air-bone gap in the lower frequencies (Fig 3B). Mastoid x-ray films showed a cloudy mastoid and middle ear on the right side and a normal mastoid and middle ear on the left side. On Nov 6, 1986, she was taken to the operating room, and the right ear was explored through a postauricular incision. After developing the tympanomeatal flap, we found a yellow cyst in the middle ear and attic extending toward the mastoid antrum. Through an atticotomy the cyst was removed and opened. Yellow granules were found in its interior. A diagnosis of cholesterol granuloma was made. An antrotomy was performed, and the antrum was found to be normal. There was a deformed malleus and incus (Fig 2A, right) that were fixed in the attic. There was no sign of a stapes, and the oval window was closed solidly by bone (Fig 2B). There was no annular ligament. At this time the tympanic membrane was grafted, and no reconstruction of the chain was performed. Six months later the right ear was operated on again, and reconstruction of the ossicular chain was accomplished as described for case 1 (Fig 2C). The postoperative audiogram is shown in Fig 3C.

Pedigree. Figure 4 shows a schematic description of the pedigree for the two patients described. The information was obtained by the senior author by interviewing the paternal grandmother, who had reared the two children since their father was killed during a street fight. Unfortunately, all members of the family were scattered in northern Brazil and could not be brought in for otologic and audiometric examination. However, we obtained a precise description of the father's congenital deformities: he had defects in the pinna and external canal on both sides that were described as identical to the defects we found in the children and was hard of hearing, as were his offspring. He had no other congenital problems.

It appears, therefore, that the anomalies came into being for the first time in the family in the father of the probands and were reproduced in his two descendants (he had no other children). The father's nine brothers and sisters were normal, and the defects did not appear in two previous generations of his numerous family.

The mother was normal, as were her 13 brothers and sisters and the maternal grandparents. There was no consanguinity between the father and mother of the probands. There were no problems during the pregnancies, nor at delivery of the two malformed children.

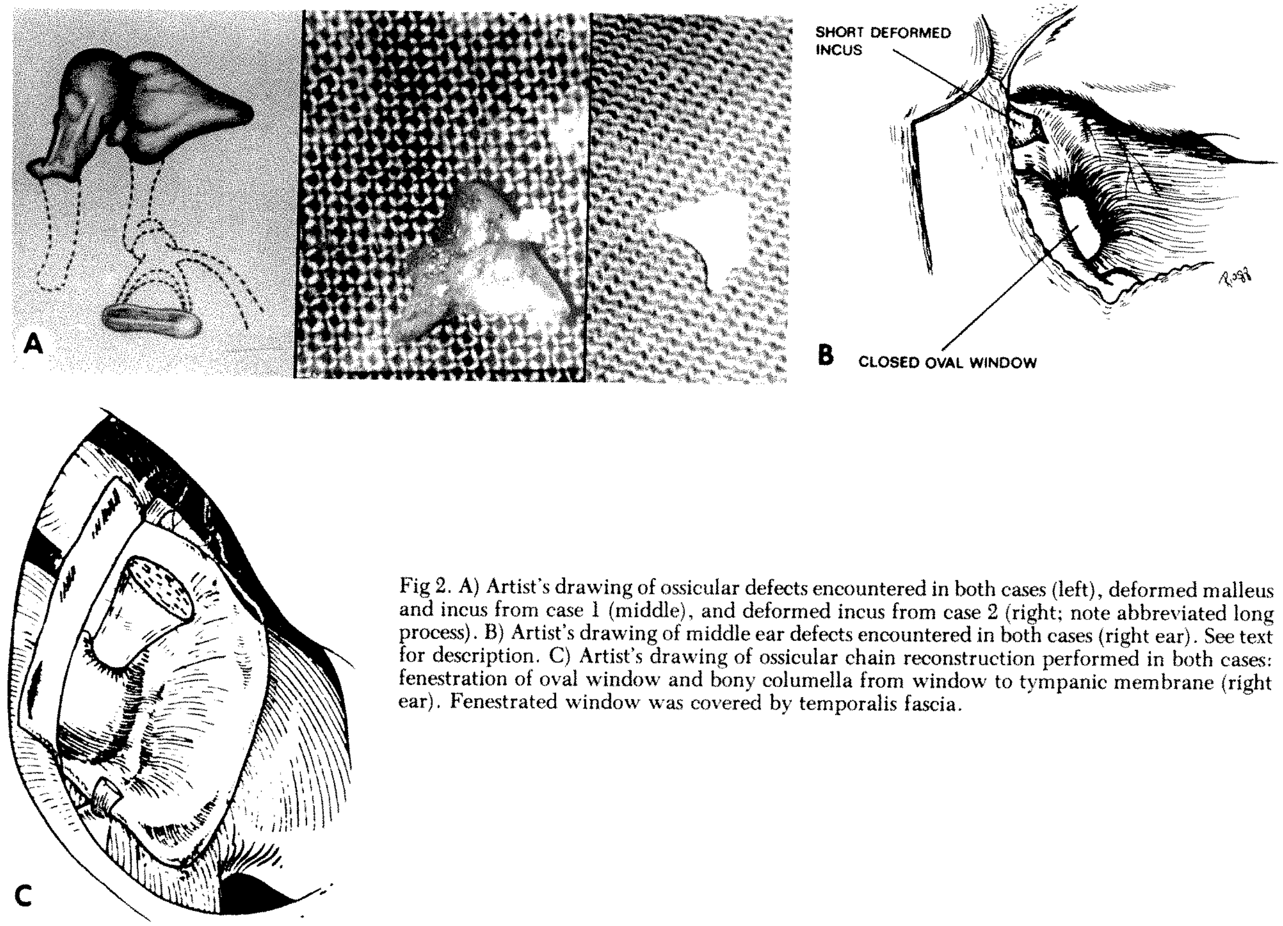

Fig 2. A) Artist's drawing of ossicular defects encountered in both cases (left), deformed malleus and incus from case 1 (middle), and deformed incus from case 2 (right; note abbreviated long process). B) Artist's drawing of middle ear defects encountered in both cases (right ear). See text for description. C) Artist's drawing of ossicular chain reconstruction performed in both cases: fenestration of oval window and bony columella from window to tympanic membrane (right ear). Fenestrated window was covered by temporalis fascia.

DISCUSSION

Ellwood et al[3] in 1968 described two siblings with microtia, external canal atresia, and hearing loss. There was a suggestion of defect in the mandibular arch (difficulty opening the mouth) and normal facial structures. They were products of a consanguineous Arab Muslim marriage. The anomalies of the ear were bilateral. Ellwood et al went on to describe two brothers from a Jewish marriage who were born with unilateral microtia and meatal atresia on the left side. As the past history was negative for ear malformations in both families and both were consanguineous marriages, it was thought that an autosomal recessive mode of inheritance was most likely.

Konigsmark et al[5] in 1972 described two siblings with microtia and external canal atresia. One had the defects on both sides; the other had a normal right side and a profound sensorineural hearing loss on the deformed left side. The child who had the anomalies bilaterally had atresia of both external canals. In the unilateral defect the external canal was stenosed but present. Even though the parents were unrelated and there was no family history of ear malformations, the authors ascribed these cases to an autosomal recessive mode of inheritance and expressed the opinion that they were representative of the same syndrome described by Ellwood et al,[3] which they suggested should be named "recessive microtia, meatal atresia and hearing loss."

Guizar-Vásquez et al[7] in 1978 described unilateral microtia and canal atresia in a mother and son. No other members of the family were affected. There were some associated anomalies of facial structures (broad nasal bridge and nose, large philtrum, and slight macrostomia), and the mother presented partial facial paralysis on the affected side. Guizar-Vásquez et al commented that the features presented in these cases were different from the known genetic syndromes associated with first- and second-arch anomalies (Treacher Collins syndrome, Goldenhar's syndrome) and postulated an autosomal dominant mode of inheritance.

Zankl and Zang[8] in 1979 described five cases of microtia and external auditory canal deformities (complete atresia in some cases, stenosis in others). There were mandibular arch defects in some instances; one patient had a cleft palate; and in patients who had middle ear surgical exploration, malformed middle ear clefts and ossicles were found. Some of these patients were born from affected parents, while others were born from normal parents. As there was no consanguinity in the family, Zankl and Zang postulated an autosomal

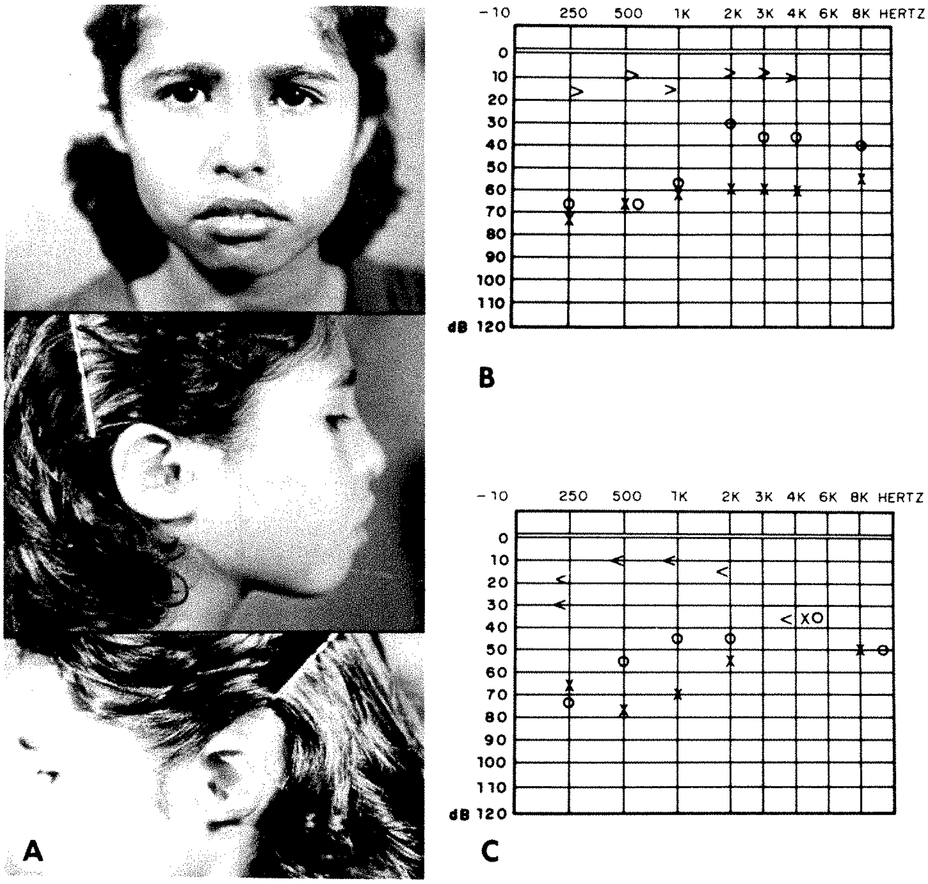

Fig 3. (Case 2) A) Bilateral microtia with no evidence of facial paralysis (top), microtia type I and stenotic external ear canals (middle and bottom). B) Preoperative audiogram. C) Postoperative audiogram.

dominant mode of inheritance with incomplete penetrance of the mutant gene.

Schmid et al[1] in 1985 described three siblings with right-sided microtia, canal atresia, and hearing loss. Two of these also had right-sided palatoplegia. As the parents were unaffected and their family was from a small community with a high rate of consanguinity, Schmid et al felt that these cases were representative of the autosomal recessive form of inheritance as described by Ellwood et al[3] and Konigsmark et al.[5]

Our cases present microtia and external canal stenosis bilaterally. These features have been described previously in cases of hereditary ear malformations. The middle ear malformations that we document have not been reported previously as inherited anomalies. The previous reports do not provide a detailed description of middle ear anomalies, even though some of the patients have undergone middle and external ear reconstruction. The most remarkable feature of the anomalies in our two cases is that they are almost identical. Except for a partial facial paralysis that was present in case 1 and absent in case 2, the anomalies of the pinna, external canal, and middle ear were the same. The patient in case 2 had an acquired ear infection in the right ear that resulted in a cholesterol granuloma, but the congenital deformities were the same as in case 1. According to the grandmother's description, the father of the probands had identical external ear deformities. All three involved members of the family had hearing losses, which were conductive in the two children. Unfortunately, we could not do an audiogram on the father.

Konigsmark and Gorlin[9] in 1976 stated that "the development and function of the ear are dependent upon hundreds or even thousands of genes interacting with each other and with the intra and extrauterine environment. The form of the pinna for example is dependent upon many genes (multifactorial inheritance) but it may be grossly altered by single gene mutation. The same applies to the external auditory canal, the ossicles, the oval window... ."

Pedigree analysis in our cases (Fig 4) points strongly to an autosomal dominant mode of inheritance: the affected father transmitted the trait to 100% of his descendants. On the other hand, the father's nine brothers and sisters were normal, and there was no notice of ear malformations in two previous generations of his very numerous family. The mother's family was unrelated to the father's and had no known affected member. We thus are led to believe that a spontaneous mutation appeared for the first time in the father of the probands and was inherited by the children in autosomal dominant fashion. The children should transmit these deformities to their descendants in the

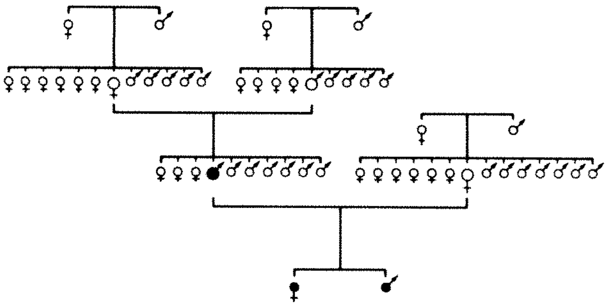

Fig 4. Schematic representation of pedigree of two siblings. Dark circles represent affected members of family. See text for detailed description.

same fashion. It will be interesting to prove or disprove this theory by studying future generations of this family.

Certainly it would be desirable to have data on physical examination and audiometry in all members of the family. However, pinna deformities and severe deafness are obvious problems that certainly would not go unnoticed by the paternal grandmother in any of her relatives.

It appears that the development of first and second branchial arch structures is dependent upon many genes. Mutations of a single gene or of combinations of genes will produce a spectrum of more or less similar malformations ranging from full-blown Treacher Collins syndrome or Goldenhar's syndrome to isolated external and middle ear malformations. Some of these mutations may be occasional and never recur. Some others occur frequently enough to justify the description of a genetic syndrome.

From a practical standpoint, the clinician who must provide genetic counseling for prospective parents who have isolated external and middle ear deformities might mention to them the possibility that even though the anomalies have appeared sporadically in their families they may be transmitted to their descendants in an autosomal dominant fashion. The probability is unknown, but we believe it to be slight.

Our experience with the surgical treatment of congenital external and middle ear malformations will be the subject of a separate report. We will offer here only a short comment on these two cases.

In the preoperative evaluation and selection of patients for surgical treatment, we have followed the guidelines recently established by De La Cruz.[10] The results in these two cases are modest, in general agreement with the experience of others.[10,11] In the process of deciding whether to operate on these patients, the surgeon should weigh the risks involved against the possible benefits, which are predictably modest. In evaluating the risks, one must be very critical of one's own skills and experience in otologic surgery. Specifically, in fenestrating a congenitally sealed oval window, the risk of excessive perilymph leak (gusher) with inner ear damage should be taken into consideration. We did not encounter this problem in the two cases described. A better result was achieved in case 1 than in case 2, and this result has been stable up to now.

Hough et al[12] have recently described clinical experience with an implantable bone conduction hearing device. Considering the lower risk involved in implanting this device, if the long-term hearing results prove better than those obtained with reconstructive surgery, it may become the treatment of choice in the future.

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RECENT MODIFICATIONS IN THYROPLASTY TYPE I

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Among thyroplasties, type I is the most frequently used for medialization of the vocal cord. Follow-up study on patients indicated that reversion of voice can occur after operation. Revision was done in five cases with improvement of voice. On the basis of this experience, modifications were made in the technique of thyroplasty type I. They include 1) cutting the calcified cartilage with minimal intervention in the soft tissue, 2) fixation of the window with a silicone plug to enhance medialization, and 3) overmedialization of the vocal cord and definition of criteria for it that can be used during surgery.

KEY WORDS — phonosurgery, thyroplasty, voice.

INTRODUCTION

Since 1972, we have performed various types of thyroplasties on over 200 patients with dysphonia.[1-4] The thyroplasty and its modifications appear to be used increasingly for vocal cord paralysis or atrophy.[5-8] The type most frequently used is thyroplasty type I, which medializes the vocal cord through a window made in the thyroid ala. On patient follow-up, we sometimes noticed slight reversion of the voice over 2 to 3 months after operation. The size of the glottal chink during phonation appeared to be parallel to the degree of dysphonia. The main factor responsible for dysphonia seemed to be atrophy of the vocal cord rather than the change in the position of the vocal cord. Manual compression of the thyroid cartilage at the window site generally improved the voice.

In an attempt to eliminate the glottal gap or to correct the concave vocal cord margin, thyroplasty was performed again on five patients. Local findings in the revision are as follows. The window site was covered with a thick semitransparent membranous tissue without any sign of inflammation. The silicone shims were found to be in the expected position at the window without any distortion, and the neighboring cartilage tissues in contact with the silicone showed no sign of erosion.

The silicone shim was replaced with a thicker silicone plug. All of the patients still showed marked improvement in voice at least 6 months postoperatively.

Some reversion of the voice can occur after thyroplasty type I. Possible factors responsible for this reversion include 1) subsidence of the vocal cord edema caused by the operation, 2) scar contracture of the tissue around the inner perichondrium of the window, 3) atrophy of the soft tissue inside the inner perichondrium due to a constant pressure by the medialized window, 4) progressive atrophy of the vocal cord due to denervation, and 5) shift of the shim or the cartilage window after operation.

From the findings on revision, it seems most likely that intraoperative edema and/or progressive denervation atrophy of the vocal cord causes the postoperative reversion of voice.

MEASURES TO PREVENT REVERSION OF VOICE

Less Edema During Surgery. In general, the longer the time required for the surgery, the greater the edema of the vocal cord, which would lead to misjudgment in adjusting medialization of the vocal cord and consequent reversion of voice. Thyroplasty type I usually takes about an hour to perform unilaterally — a little less in a woman and a little more in a man with a densely calcified larynx. Rough prefabrication of a silicone plug curtails the time of surgery.

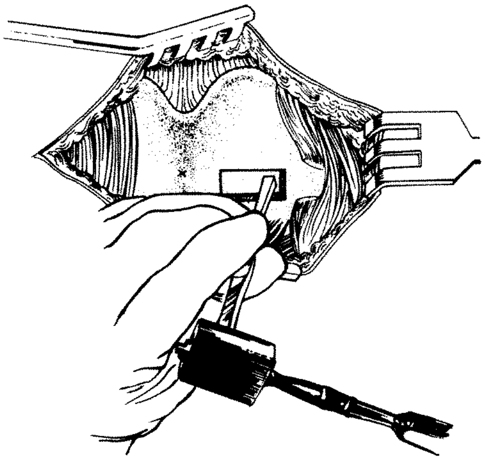

Fig 1. Technique of cutting cartilage window. When thyroid cartilage is calcified, most of cartilage layer is cut first with very fine bur, and last thin layer may be gently cracked with bone hemostatic chisel.

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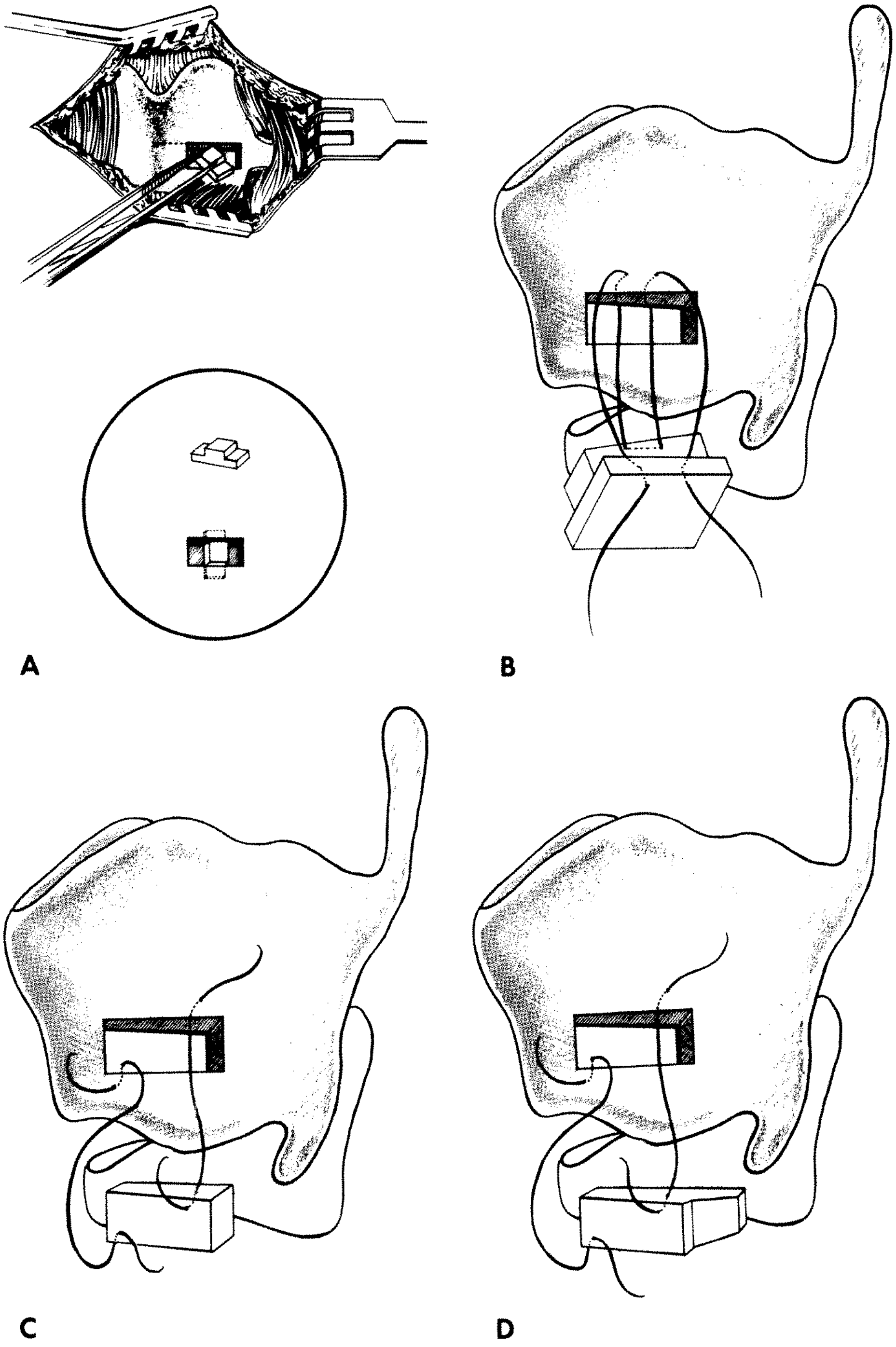

Fig 2. Window fixation. A) With silicone shim. B) With flanged plug. Suturing technique is more complicated. C) With simple plug made to size that fits window somewhat tightly so that almost no suturing is necessary. D) With plug that has wedge-shaped extension to enhance medialization of posterior portion of vocal cord.

Much more important than the time is how to make a window in the thyroid ala with minimal surgical intervention, especially without entering the inner perichondrium. For cutting a thyroid cartilage in a state of advanced calcification, use of a very fine bur (Maillefer 700 [Switzerland]) is essential. The safest method is to cut 80% to 90% of the entire thickness, leaving a paper-thin layer for the final cut with a very fine chisel or fine raspatory. The last thin layer may be cracked with a bone hemostatic chisel that is hammered gently at the window (Fig 1). Thrombin powder or hemostatic collagen should be applied to control even minute bleeding. The window must be free enough to make medialization of the vocal cord adjustable in a correct and delicate manner.

Fixation of Window. Figure 2A shows a window fixed in a depressed position with a silicone shim. When the shim is placed in the window, it tends to bend, making depression of the window less effective. For firmer fixation, a silicone plug has been found more useful than the shim. Various types of plugs have been tried (Fig 2B,C) with or without flanges. The one we use most frequently at present is a simple plug without flanges. It is made to a size that fits the window just a little tightly, so that no fixation sutures are necessary in most cases. One or two sutures may be used to secure the fixation.

The thickness of the plug is most frequently 3 mm anteriorly and 4 to 5 mm posteriorly (Fig 2C). It may have a wedge-shaped extension posteriorly that is placed beneath the unfenestrated posterior part of the thyroid ala in order to enhance medialization of the posterior portion of the vocal cord (Fig 2D).

Overmedialization. Since some degree of edema will inevitably develop in the vocal cord during surgery, slight overmedialization generally is recommended. So far we have never experienced a case in which excessive medialization of the vocal cord remained months after operation.

Intraoperative judgments on medialization are not always easy to make, though. An apparent glottal chink on phonation revealed on intraoperative videoendoscopy and a breathy quality of voice are unmistakable signs of undercorrection. However, when the voice sounds almost normal and the glottal closure appears complete, whether further medialization, probably by a fraction of a millimeter, should be done or not often presents a difficult decision. A clear but slightly weak voice is likely to indicate imperfect glottal closure of a slight degree, just as a clear falsetto always indicates a narrow glottal slit. Our current tactic for determining the proper slight overcorrection is first to achieve a clear, almost normal voice, then to push the window down further until the voice becomes just slightly rough in quality. Actually, the decision requires considerable knowledge of voice physiology and surgical experience. Since we adopted this policy of overcorrection 4 years ago, we have had no cases of apparent excessive correction in patients evaluated approximately 3 months after operation. Long-lasting overcorrection seems less likely to happen if it is done carefully. Neither dyspnea nor stridor occurred postoperatively in any case in which overmedialization was attempted. In women, in whom the fenestration procedure in the thyroid ala usually takes around half an hour, with less soft tissue intervention, this compensation for probable edema may not be necessary, or when made, may be to a much lesser extent.

In a previous paper,[2] we reported that the prognosis of thyroplasty type I in cases of atrophy or a concave edge of the vocal cord is not as good as in vocal cord paralysis. The fenestration procedure to medialize the vocal cord is generally much less effective when the vocal cord is mobile than when it is not. For vocal cord atrophy, therefore, bilateral forceful medialization of the vocal cord usually is required. It can be accomplished without much fear of complication such as dyspnea. Results of surgery in vocal cord atrophy have been much improved by the bilateral medialization policy.

Either thyroplasty type I or arytenoid adduction[9] is selected currently for medialization of the vocal cord, mostly depending on the width of the glottal chink. Arytenoid adduction brings about more effective adduction of the vocal cord. However, with the introduction of more effective and reliable means to medialize the vocal cord, for the most part by fixation, thyroplasty type I, which is much simpler and easier to perform than arytenoid adduction, now is being used more frequently than before, even for a fairly wide glottal chink.

In summary, some modifications were made after reflection on the cases of postoperative reversion of voice and local findings in the reviewed cases. The modifications include the manner of fenestration, fixation of the window with a silicone plug, and overmedialization.

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REVIEW OF NEUROENDOCRINE CARCINOMAS OF THE LARYNX

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Neuroendocrine carcinomas of the larynx are uncommon tumors of considerable scientific interest and clinical importance. They include typical carcinoid tumors, atypical carcinoid tumors, and small cell neuroendocrine carcinomas. This paper considers these neoplasms from a personal experience and reviews the relevant medical literature. About 200 cases of neuroendocrine carcinomas of the larynx have been reported. The diagnosis is based on light microscopy and is confirmed by ultrastructural evidence of neurosecretory granules. Histochemical and immunocytochemical investigations may support it. Paraneoplastic syndromes associated with laryngeal neuroendocrine carcinomas have been reported occasionally. The histogenesis, treatment, and prognosis of these lesions also are discussed.

KEY WORDS — atypical carcinoid, small cell neuroendocrine carcinoma, typical carcinoid.

Neuroendocrine carcinomas of the larynx include the typical carcinoid tumors, atypical carcinoid tumors, and small cell neuroendocrine carcinomas.

The neuroendocrine features shared by these tumors include the presence of neurosecretory cytoplasmic granules, which may be demonstrated by special histochemical stains or transmission electron microscopy, and the immunohistochemical identification of a variety of immunoactive peptides within the tumor cells. Despite their similarities, small cell neuroendocrine carcinomas and carcinoid tumors are clinically distinct neoplasms with different treatment regimens.[1]

Our purpose here is not to present additional cases of neuroendocrine carcinomas of the larynx, but rather to discuss these neoplasms in the light of personal experience and to review the medical literature.

NOMENCLATURE

Recently, the generic term neuroendocrine carcinoma has been used to designate typical carcinoid tumors, atypical carcinoid tumors, and small cell neuroendocrine carcinomas. Woodruff et al[2] suggested a division of neuroendocrine carcinomas of the larynx into two main types: small cell neuroendocrine carcinomas and large cell neuroendocrine carcinomas. The latter might supplant the well-recognized term carcinoid. Some authors describe typical and atypical carcinoid tumors as non–small cell neuroendocrine carcinomas. Although the term neuroendocrine carcinoma offers a unifying concept, we prefer to use the familiar diagnostic terms typical carcinoid tumor, atypical carcinoid tumor, and small cell neuroendocrine carcinoma.[3] Table 1 indicates the classification of the laryngeal neuroendocrine carcinomas.

INCIDENCE

Neuroendocrine carcinomas of the larynx are uncommon, and their incidence is difficult to assess. Goldman et al[4] presented the first description of an atypical carcinoid tumor of the larynx in 1969, and Olofsson and van Nostrand[5] that of a small cell (oat cell) carcinoma in 1972. In 1980, Markel et al[6] also reported the first well-documented case of laryngeal typical carcinoid tumor. Another case was reported by Gehanno et al[7] in the same year, but they provided no histologic documentation. The total number of cases reported in the world literature may be about 200,[1-41] 79 of which are carcinoid tumors.

In the Department of Otolaryngology, University of Padua, 18 cases of laryngeal neuroendocrine carcinoma were identified over a 22-year period (1966 to 1987), 17 of which were small cell neuroendocrine carcinomas and one of which was an atypical carcinoid tumor, in a series of 3,647 primary and secondary laryngeal malignant neoplasms.

Neuroendocrine carcinomas form the largest group of nonepidermoid carcinomas of the larynx.[2] The occurrence of these neoplasms in the larynx may not be as rare as was thought previously.

PATHOLOGIC FEATURES

Typical Carcinoid Tumor. This represents the rarest neuroendocrine carcinoma of the larynx[25] and is the equivalent of the typical pulmonary carcinoid tumor.

Grossly, the tumor appears as a submucosal, unencapsulated growth. Microscopically, it is composed of sheets and nests of uniform cells with centrally placed, small, round or oval nuclei in a poorly delineated clear or slightly granular eosinophilic

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TABLE 1. TAXONOMY OF LARYNGEAL NEUROENDOCRINE CARCINOMAS

- Typical carcinoid (or mature carcinoid)
- Atypical carcinoid (or malignant carcinoid)
- Small cell neuroendocrine carcinoma
    - Oat cell type
    - Intermediate cell type
    - Combined cell type

cytoplasm (Fig 1). There are occasional mitoses. The neoplasm may present ribbonlike structures, glandular lumens, and rosettelike structures. The fibrous stroma is frequently hyalinized. Amyloid may be present. The neoplasm may take on a distinct oncocytic appearance. This variant is composed of large cells with abundant eosinophilic, finely granular cytoplasm with a small, centrally located hyperchromatic nucleus. Ultrastructurally, the cells show marked mitochondrial hyperplasia. Argyrophil stains (Grimelius, Sevier-Munger, Pascual, Churukian-Schenk, Bodian, Wilder) are usually positive, while argentaffin stains (Fontana-Masson, Masson-Hamperl, Diazo, Schmorl) are often negative. Ultrastructural studies demonstrate, without exception, the presence of numerous round and oval neurosecretory granules in the cytoplasm. The membrane-bound granules have an electron-dense core separated from the membrane by a clear space. Immunoperoxidase stains for neuron-specific enolase (NSE), chromogranin, serotonin, keratin, and somatostatin may reveal cytoplasmic positivity.[25,29]

Atypical Carcinoid Tumor. Grossly, this neoplasm has no distinctive features, and it is not possible to distinguish it clinically from a squamous carcinoma. Histologically, it has the appearance of a carcinoid tumor as described above, but shows frequent mitoses, hypercellularity, focal necrosis, loss of architecture, nuclear and cytologic pleomorphism, and reduced cytoplasm (Fig 2A,B). This tumor also may produce amyloid. Oncocytic and/or oncocytoid changes sometimes may occur (Fig 2C). Rarely, mucinous changes may be present. Morphologic diagnosis is based primarily on conventional light microscopy and confirmed by histochemical, immunohistochemical (Fig 3A), and ultrastructural investigations (Fig 3B). Argyrophil stains may reveal positively stained granules in the cytoplasm of tumor cells (Fig 3C), but argentaffin stains are usually negative. Chromogranin, serotonin, calcitonin, somatostatin, ACTH, Leu 7, carcinoembryonic antigen, NSE, cytokeratins, gastrin, glucagon, growth hormone, met-enkephalin, and human chorionic gonadotropin can be demonstrated immunohistochemically in this tumor (Table 2[1,2,8-10,25,29,31-39]). Electron microscopy reveals neurosecretory granules, but in smaller quantity than in the typical carcinoid tumor.

Small Cell Neuroendocrine Carcinoma. Small cell neuroendocrine carcinomas of the larynx may be divided[40] into oat cell carcinoma (Fig 4A), intermediate cell type (Fig 4B), and combined small cell carcinoma (Fig 4C). Oat cell carcinoma is composed of uniform small cells with sparse cytoplasm. The cells of the intermediate type of small cell carcinoma are similar except that some may exhibit a more abundant cytoplasm. Combined small cell carcinomas are tumors in which there is a definite component of small cell carcinoma (oat cell carcinoma or intermediate cell type), together with squamous cell carcinoma and/or adenocarcinoma. Mitoses are numerous and vascular (Fig 5A); perineural (Fig 5B) and skeletal muscle invasion is found commonly. Rarely, glandular structures may be present (Fig 5C). Grimelius and Fontana-Masson stains for argyrophilic and argentaffin cells usually

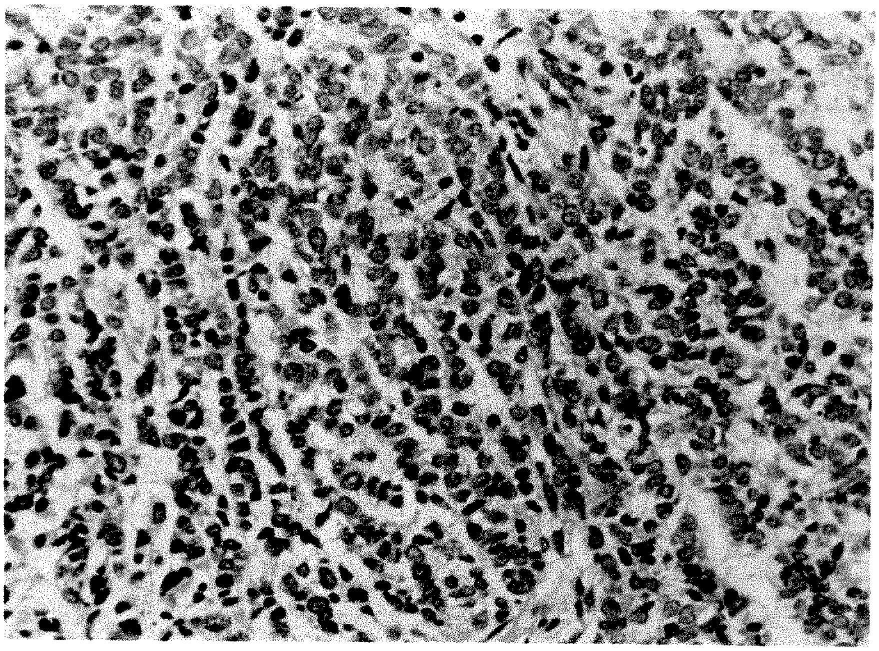

Fig 1. Typical carcinoid tumor of larynx of trabecular pattern composed of cuboidal cells with round to ovoid nuclei (H & E, original x400).

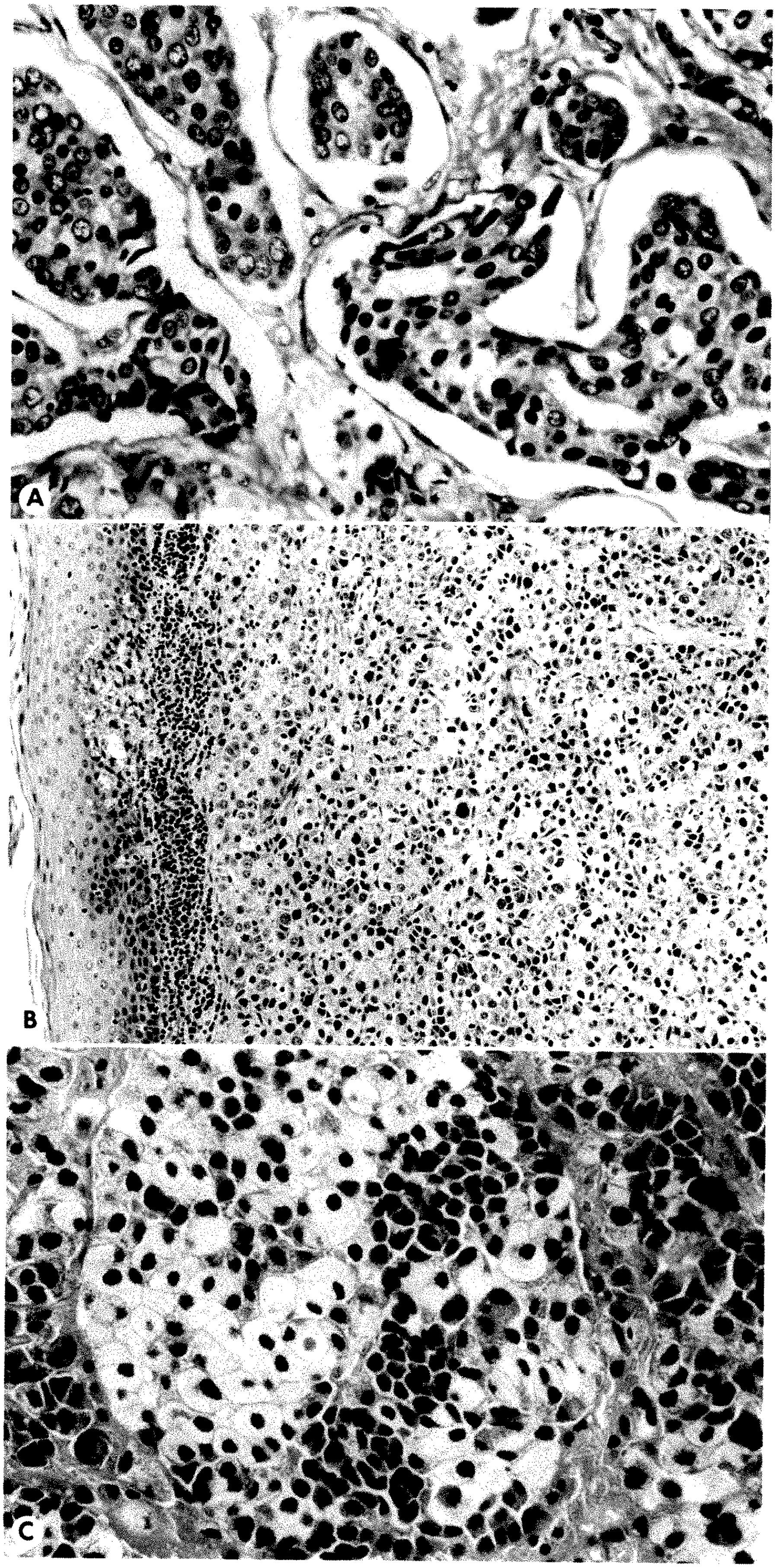

Fig 2. Atypical carcinoid of larynx. A) Displaying mosaic pattern (H & E, original x400). B) Forming dense infiltrate beneath laryngeal epithelium (H & E, original x160). Note considerable nuclear irregularity. C) Showing oncocytoid features (H & E, original x400).

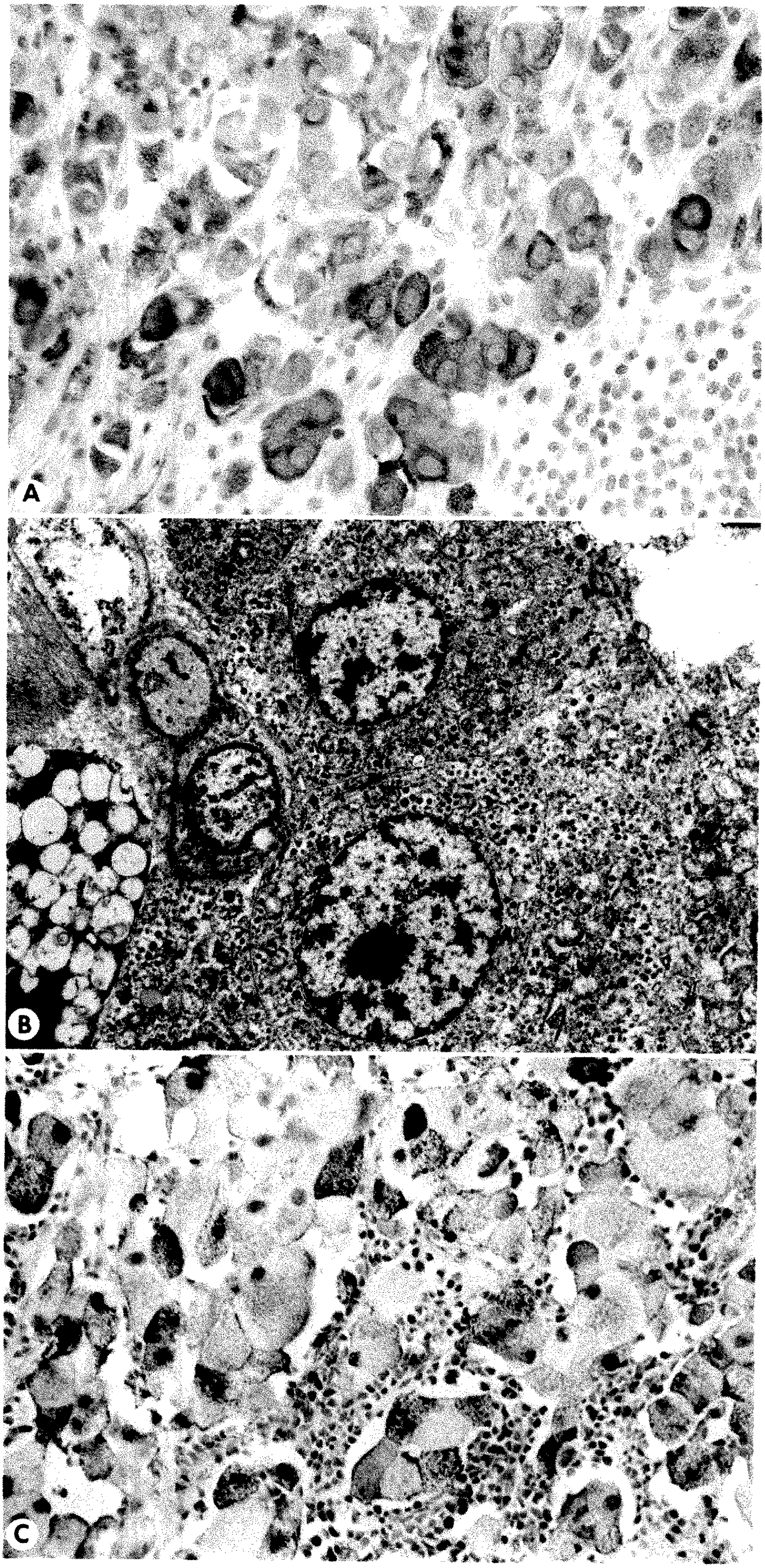

Fig 3. Atypical carcinoid of larynx. A) Showing positive immunoperoxidase reaction for calcitonin (original x400). B) Showing numerous neurosecretory granules on electron microscopy (uranyl acetate and lead citrate, original x7,200). C) Forming secondaries in subcutaneous tissues of neck (original x400). Note Grimelius-positive argyrophilic cells.

TABLE 2. POSITIVE IMMUNOHISTOCHEMICAL REACTIONS IN LARYNGEAL CARCINOIDS

Authors	*Antisera*
Gould et al[31]*	Calcitonin, somatostatin, ACTH
Gould[32]*	Calcitonin, somatostatin, ACTH
Paladugu et al[33]*	Calcitonin, somatostatin, ACTH
Sweeney et al[34]†	Calcitonin, CEA
Cefis et al[35]§	Calcitonin, ACTH, α-hCG
Solcia et al[9]§	Calcitonin, ACTH, α-hCG
Pages et al[36]	ACTH
Luboinski et al[8]	Calcitonin, CEA, ACTH, Leu 7 (HNK-1)
Woodruff et al[2]	Calcitonin, somatostatin, serotonin, NSE, CEA, hCG
Baugh et al[1]	Calcitonin, serotonin, chromogranin
Patterson and Yarington[37]	Chromogranin
Porto et al[38]	Calcitonin, NSE, serotonin, ACTH, met-enkephalin, chromogranin, high molecular weight keratin, low molecular weight keratin
Ferlito et al[25]	Calcitonin, NSE, chromogranin, cytokeratin, gastrin, somatostatin, glucagon, GH
Googe et al[29]	Serotonin, chromogranin, NSE, CEA, keratin
Wick et al[10]	Chromogranin

ACTH — adrenocorticotropic hormone, CEA — carcinoembryonic antigen, α-hCG — alpha chain of human chorionic gonadotropin, NSE — neuron-specific enolase, hCG — human chorionic gonadotropin, GH — growth hormone.

*Authors refer to same patient.

†Duvall et al[39] and Woodruff et al[2] consider this case as laryngeal atypical carcinoid, while Sweeney et al[34] present it as ectopic thyroid medullary carcinoma of larynx.

§Authors refer to same patient.

are negative, probably because of the paucity of neurosecretory granules revealed by electron microscopy. Immunoreactive studies may yield positive reactions for calcitonin, keratin, somatostatin, carcinoembryonic antigen, NSE, chromogranin, ACTH, C-flanking peptide of human probombesin, serotonin, protein gene product 9·5, neurotensin, β-endorphin, and gastrin-releasing polypeptide (GRP) (Table 3[2,14,15,29,31,32,41]).

HISTOGENESIS

The histogenesis of neuroendocrine carcinomas of the larynx has remained obscure. They are thought to originate from endocrine cells or argyrophilic Kulchitsky's cells (K cells) normally found in animal[42-44] and human[45] laryngeal mucosa, so they are included in the group of tumors of the diffuse endocrine system, the so-called APUD system (amine precursor uptake and decarboxylation). It was originally suggested that all APUD cells originate from the neural crest,[46] but other data support an endodermal origin of the APUD cells of the digestive and respiratory tract.[47]

It is also possible that the neoplasms arise from normally nonargyrophilic but pluripotential indifferent cells in the seromucous gland-duct apparatus.[2] The coexistence of tonofilaments, cilia, desmosomes, neurosecretory granules, and mucin granules within single tumor cells supports the hypothesis that the neuroendocrine tumors arise from a common primitive and pluripotential stem cell, rather than from a specific neuroendocrine precursor.

NONMETASTATIC OR PARANEOPLASTIC SYNDROMES ASSOCIATED WITH LARYNGEAL NEUROENDOCRINE CARCINOMAS

Paraneoplastic syndromes associated with laryngeal small cell neuroendocrine carcinomas have been reported. In 1979, Trotoux et al[48] described the Schwartz-Bartter syndrome (inappropriate secretion of antidiuretic hormone) in a 61-year-old man that led to the detection of a small cell carcinoma in the subglottic region of this patient. This case demonstrated the hormone-secreting property of the cells of this tumor.

In 1984, Medina et al[49] reported a case of primary small cell neuroendocrine carcinoma of the larynx associated with clinical and electromyographic evidence of the myasthenic syndrome (Eaton-Lambert syndrome), which was first described by Eaton and Lambert[50] in 1957.

In 1985, Bishop et al[14] described a case of laryngeal oat cell carcinoma with the ectopic ACTH syndrome. They found ACTH, GRP, NSE, β-endorphin, calcitonin, and keratin in the tumor cell cytoplasm by indirect immunoperoxidase techniques. Adrenocorticotropic hormone production therefore may occur in laryngeal small cell carcinoma, as in small cell lung cancer. A paraneoplastic syndrome may be the first indication of an underlying laryngeal small cell carcinoma.

The classical carcinoid syndrome and other ectopic hormonal syndromes have not been reported in typical and atypical carcinoid tumors of the larynx, although the clinical history of the second case report by Baugh et al[1] refers to "abdominal cramping, distension, alternating diarrhea and constipation, and a generalized warm feeling" — recognized symptoms of the carcinoid syndrome.[25] This syndrome has been observed with oat cell carcinomas and carcinoids of the lung.

The nonmetastatic syndromes associated with laryngeal neuroendocrine carcinomas are summarized in Table 4.[1,14,48,49] None of the patients with paraneoplastic syndromes survived. These syndromes are not due to direct organ invasion, but they are caused by substances elaborated by the distant tumor. Such syndromes may precede the presentation of the cancer by many months or even occasionally by several years. Both the hormones and the antibodies share the property of distant action from their sites of synthesis.

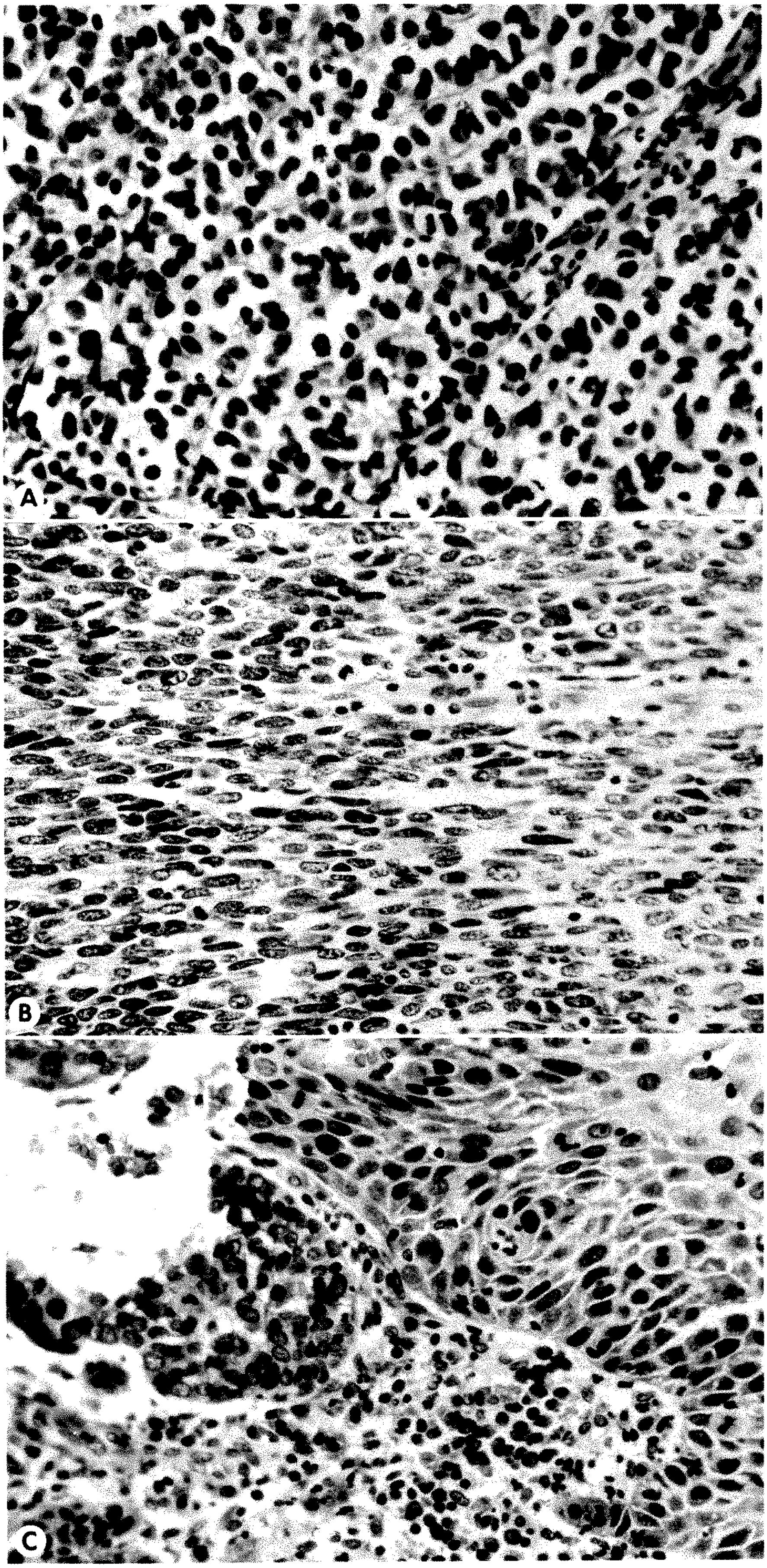

Fig 4. Small cell neuroendocrine carcinoma of larynx (H & E, original x400). A) Composed of uniform small cells with hyperchromatic nuclei and scanty cytoplasm. B) Intermediate type, composed of fusiform cells. C) Combined type. Note simultaneous squamous cell carcinoma adjacent to small cell carcinoma.

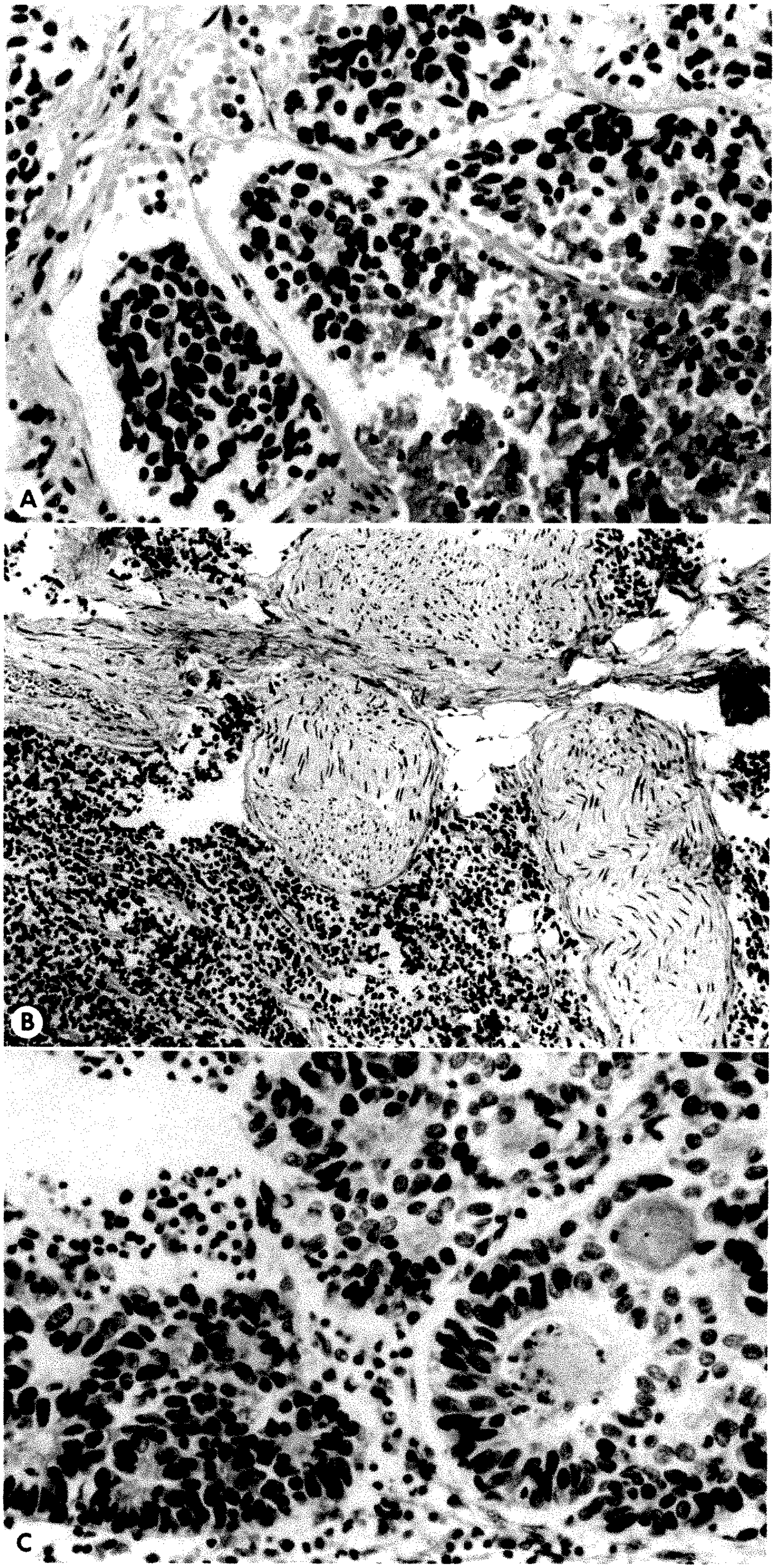

Fig 5. Small cell neuroendocrine carcinoma of larynx. A) Showing vascular invasion (H & E, original x400). B) Showing perineural space invasion (H & E, original x160). C) Forming glandular structures (H & E, original x400).

TABLE 3. POSITIVE IMMUNOHISTOCHEMICAL REACTIONS IN LARYNGEAL SMALL CELL NEUROENDOCRINE CARCINOMAS

Authors	*Antisera*
Gould et al[31]*	Calcitonin
Gould[32]*	Calcitonin, somatostatin
Bishop et al[14]	ACTH, β-endorphin, GRP, calcitonin, neurotensin, NSE, keratin
Weidauer et al[41]	Calcitonin, NSE
Woodruff et al[2]	NSE, CEA, serotonin
Springall et al[15]	NSE, PGP 9·5, bombesin, CFB
Googe et al[29]	Serotonin, chromogranin, NSE, CEA, keratin, bombesin

ACTH — adrenocorticotropic hormone, GRP — gastrin-releasing polypeptide, NSE — neuron-specific enolase, CEA — carcinoembryonic antigen, PGP 9·5 — protein gene product, CFB — C-flanking peptide of human probombesin.

*Authors refer to same patient.

TABLE 4. PARANEOPLASTIC SYNDROMES ASSOCIATED WITH LARYNGEAL NEUROENDOCRINE CARCINOMAS

Syndrome	*Type of Tumor*	*Authors*
SIADH	Small cell neuroendocrine carcinoma	Trotoux et al[48]
Eaton-Lambert	Small cell neuroendocrine carcinoma	Medina et al[49]
ACTH	Small cell neuroendocrine carcinoma	Bishop et al[14]
Carcinoid	Atypical carcinoid tumor	Baugh et al[1]

SIADH — syndrome of inappropriate antidiuretic hormone, ACTH — adrenocorticotropic hormone.

DIAGNOSIS AND DIFFERENTIAL DIAGNOSIS

The diagnosis of neuroendocrine carcinomas is based essentially on the microscopic appearance of the lesion confirmed by ultrastructural evidence of neurosecretory granules, assisted by histochemical and immunocytochemical investigations. Earlier studies of these lesions used no special immunocytochemical methods or electron microscopy. Marked elevation of 5-hydroxyindoleacetic acid caused by impaired tryptophan metabolism is considered pathognomonic for carcinoid tumor.

In classifying laryngeal neuroendocrine carcinomas, the distinction between typical carcinoid tumor, atypical carcinoid tumor, and small cell neuroendocrine carcinoma is of paramount and prognostic importance. Since typical carcinoid tumors and small cell neuroendocrine carcinomas probably occupy the two ends of a spectrum of neoplasms with different degrees of neuroendocrine differentiation, the differential diagnosis may present a particular dilemma. Some neuroendocrine tumors are composed of an admixture of small and large cells (Fig 6). Table 5 illustrates the differential comparative findings of neuroendocrine carcinomas of the larynx.

The intermediate form of small cell carcinoma often resembles an atypical carcinoid tumor and must be distinguished from it. The lack of argyrophilia, the nuclear characteristics, the lack of large or prominent nucleoli, the relative paucity of dense core granules, and large areas of necrosis may assist in the differential diagnosis.

Neuroendocrine carcinomas occurring in the larynx may be confused with metastatic small cell carcinomas of the lung, but this possibility is extremely rare, and only one case was found in a recent review of the literature.[51]

PROGNOSIS

The prognosis of typical carcinoid tumors of the larynx is favorable. We identified eight patients with this lesion in the literature,[25.29] six of whom are still living and are clinically disease free (1.5, 2, 2, 3.6, 5.6, and 8 years after diagnosis, respectively).

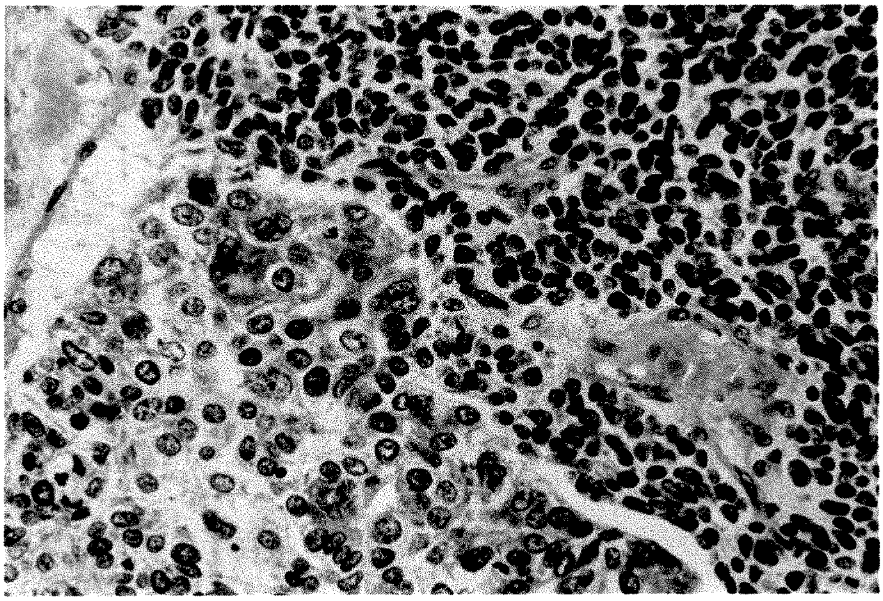

Fig 6. Neuroendocrine carcinoma of larynx. Note small and large tumor cells (H & E, original x400).

TABLE 5. COMPARATIVE FINDINGS IN LARYNGEAL NEUROENDOCRINE CARCINOMAS

Features	*Typical Carcinoid Tumor*	*Atypical Carcinoid Tumor*	*Small Cell Neuroendocrine Carcinoma*
Architecture	Organoid	Organoid	Solid
Cellular pattern	Orderly	Disorganized	Disorganized
Cellular pleomorphism	Unusual, focal	Common	Common, diffuse
Nuclear hyperchromasia	Slight	Marked	Prominent
Mitoses	Absent	Scanty	Abundant
Crush phenomenon	Absent	Absent	Prominent
Necrosis	Absent	Focal	Abundant
Oncocytic feature	May be present	May be present	Absent
Azzopardi's effect	Absent	Absent	Present
Neurosecretory granules	Numerous	Less numerous	Sparse
Size of neurosecretory granules	Average 110-140 nm	Average 80-140 nm	Average 50-200 nm
Argyrophilia	Positive	Variable	Sparse
Argentaffinity	Rare	Rare	Absent
Vascular invasion	Absent	Present	Present
Metastases	Rare	Frequent	Frequent
Clinical behavior	Benign	Malignant	Malignant

Information taken from Ferlito et al.[25]

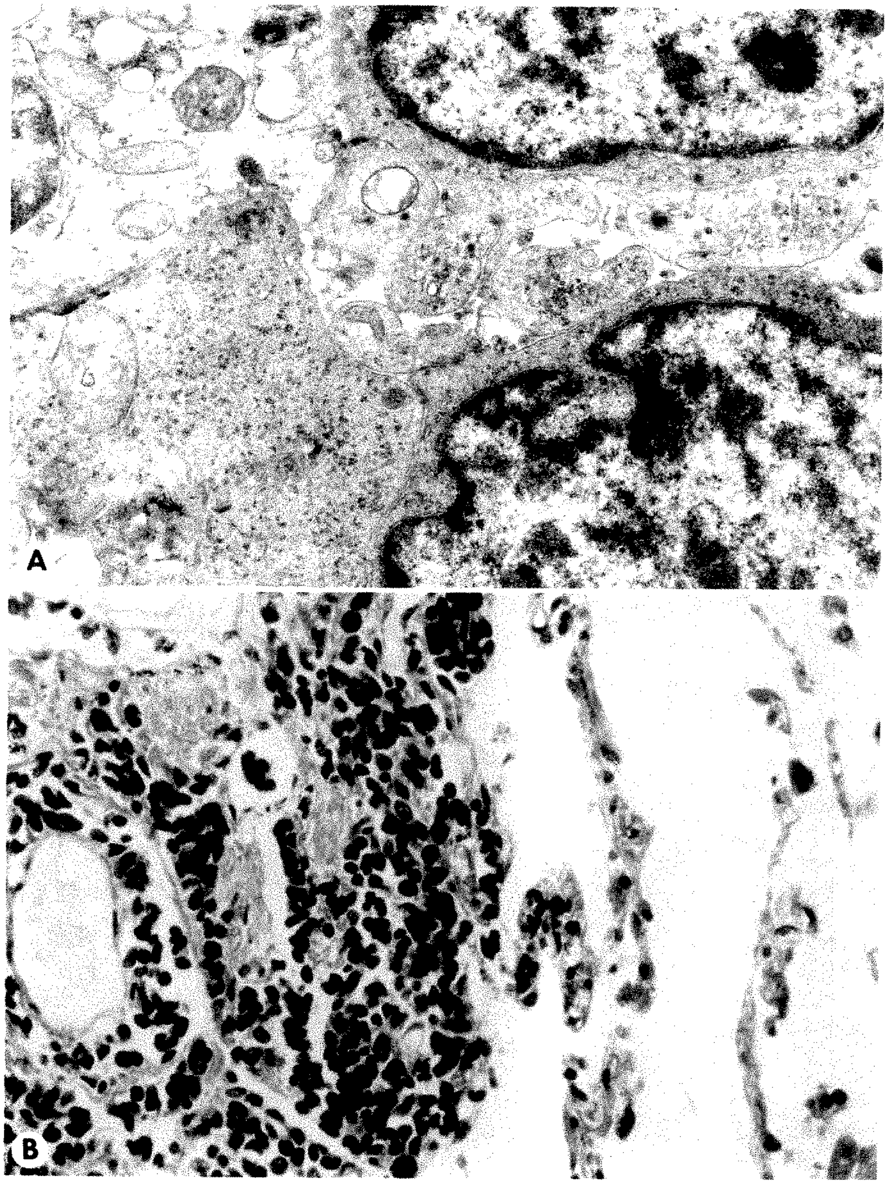

Fig 7. Metastases in patients with small cell neuroendocrine carcinoma of larynx. A) Lymph node secondary (uranyl acetate and lead citrate, original x21,000). Some neurosecretory granules are present in cytoplasm. B) Microembolic metastases in lung (H & E, original x400). Autopsy revealed secondaries in liver, mediastinal and abdominal lymph nodes, and subcutaneous tissues.

Two patients died of other causes (one was the victim of an automobile accident, and the other died of hematemesis from esophageal varices and cirrhosis of the liver). There was no evidence of tumor at autopsy in either of these cases. Metastases were absent in all eight cases.

In contrast, the clinical behavior of an atypical carcinoid tumor is aggressive. Cervical lymph nodes were involved by the tumor in about 80% of the reported cases. Other sites of metastases included skin, subcutaneous tissues, distant lymph nodes, lung, mediastinum, bones, liver, heart, pancreas, diaphragm, peritoneum, gastrointestinal tract, prostate, breast, brain, and pleura.

The prognosis of atypical laryngeal carcinoid tumors appears to be generally poor, but not as poor as that of the relatively more common and aggressive small cell neuroendocrine carcinoma, which differs from other types of laryngeal cancer in its propensity for early development of local and distant metastases and its rapidly fatal clinical course. The most common sites of metastatic spread of this highly aggressive neoplasm are cervical lymph nodes (Fig 7A), liver, lung (Fig 7B), bone, and bone marrow.

TREATMENT

As a general rule, surgical excision is the treatment of choice for typical and atypical laryngeal carcinoid tumors. Conservative laryngeal surgery should be employed if the tumor can be removed adequately.[1] Large tumors may require total laryngectomy. Neck dissection also should be performed in atypical carcinoid tumor because of the high likelihood of cervical lymph node metastases.[52] The best palliative treatment for distant metastases is surgical excision, whenever possible, as this can relieve the pain caused by subcutaneous nodules. Radiotherapy has been used without observable effect in preoperative, postoperative, and primary modalities.[53] Currently available chemotherapeutic options are inadequate. Horikawa and Matsubara[54] have used hyperthermia without success.

Systemic polychemotherapy with irradiation is the treatment of choice for small cell neuroendocrine carcinomas of the larynx.[8,13,21] Commonly used agents include cyclophosphamide, doxorubicin hydrochloride, vincristine sulfate, methotrexate, and lomustine.[13] Irradiation alone has been used successfully to control limited neoplasms. Radical surgical procedures have failed in the majority of cases reported.

Cerebral metastases are rare and occur usually as a terminal event. Prophylactic cranial irradiation may reduce the incidence of brain metastases, but does not enhance survival in small cell lung cancer.[55]

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ADDENDUM

Since submission of this article, the following papers have appeared in the literature: 1) Wenig BM, Hyams VJ, Heffner DK. Moderately differentiated neuroendocrine carcinoma of the larynx. A clinicopathologic study of 54 cases. Cancer 1988;62:2658-76. 2) Welkoborsky HJ, Sorger K, Moll R, Collo D. Primäres Larynxkarzinoid. Fallvorstellung und Literaturübersicht. Laryngol Rhinol Otol 1988;67:559-63.

Ann Otol Rhinol Laryngol 98:1989

IMPROVED SURGICAL TECHNIQUE FOR EPIDERMOID CYSTS OF THE VOCAL FOLD

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An improved surgical technique for epidermoid cysts of the vocal fold is presented. This technique employs a specially designed double-bladed elevator. Following betamethasone injection around the cyst, an incision is made posterior to the cyst at its mediolateral midpoint. The incision is extended anteriorly over the cyst with the use of a double-bladed elevator. The cyst then is elevated carefully from the surrounding tissue and removed. A single incision line on the upper aspect of the vocal fold should be the result. Eight patients were operated on with the present technique. The voice was improved postoperatively in all patients. The voice improvement was reflected objectively in stroboscopic findings, maximum phonation time, airflow rate, fundamental frequency and intensity of phonation, and results of acoustic analyses of voice.

KEY WORDS — epidermoid cyst, surgery, vocal fold.

An ideal treatment for epidermoid cysts of the vocal fold is to enucleate the cysts with minimal surgical intervention in the neighboring normal tissue. This is not always an easy task. Cysts are covered with very thin epithelium, they are usually ballooned with caseous contents, their capsule is thin, and a part of the cysts occasionally enters the vocal ligament. These conditions tend to cause rupture of the cystic wall during operation. If the cystic wall has been ruptured, it is very difficult to remove the cyst completely without concomitant removal of the covering epithelium and/or significant injury to the lamina propria of the mucosa.

This paper describes an improved technique for surgical removal of epidermoid cysts of the vocal fold. It assures a successful enucleation of cysts with minimal surgical derangement of vocal fold tissue.

SURGICAL TECHNIQUE

The surgery is conducted with the patient under general anesthesia. An operating microscope is used. Epidermoid cysts usually are located in Reinke's space (Fig 1A). First, betamethasone solution is injected into Reinke's space around the cyst. The injection facilitates elevation of the cyst and may minimize postoperative tissue reaction. When a dilated vessel is located above the cyst, it is cauterized anterior or posterior to the cyst in order to minimize bleeding during surgery.

A small epithelial incision is made first immediately posterior to the cyst at the mediolateral midpoint of the cyst (Fig 2A). Care should be taken not to make the incision too lateral or too medial from the midpoint. If the incision is made away from the midpoint, elevation of the covering epithelium from the cystic wall is often difficult. A specially designed elevator is inserted into the incision (Fig 2B). This elevator consists of two thin metal blades at the tip (Fig 3). The blades are opened gently in the incision. This causes an extension of the epitheli-

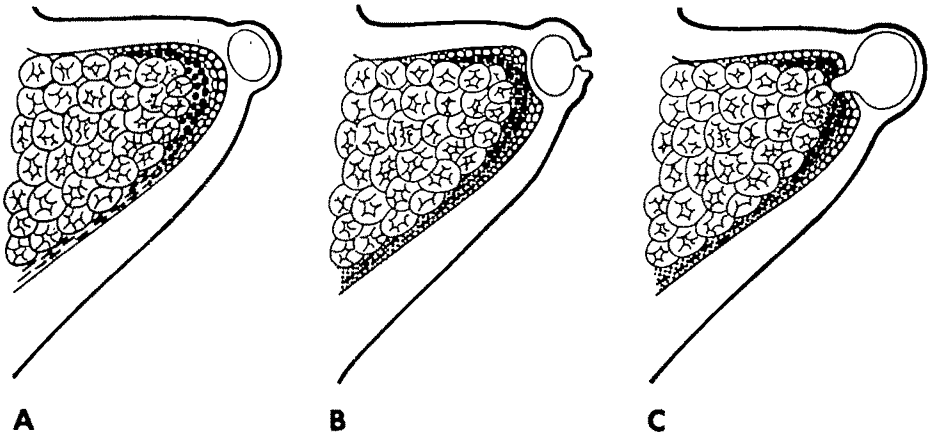

Fig 1. Schematic presentation of location of epidermoid cyst. A) Commonest type of cyst, in Reinke's space. B) Cyst connected to sulcus vocalis. C) Cyst partly entering vocal ligament.

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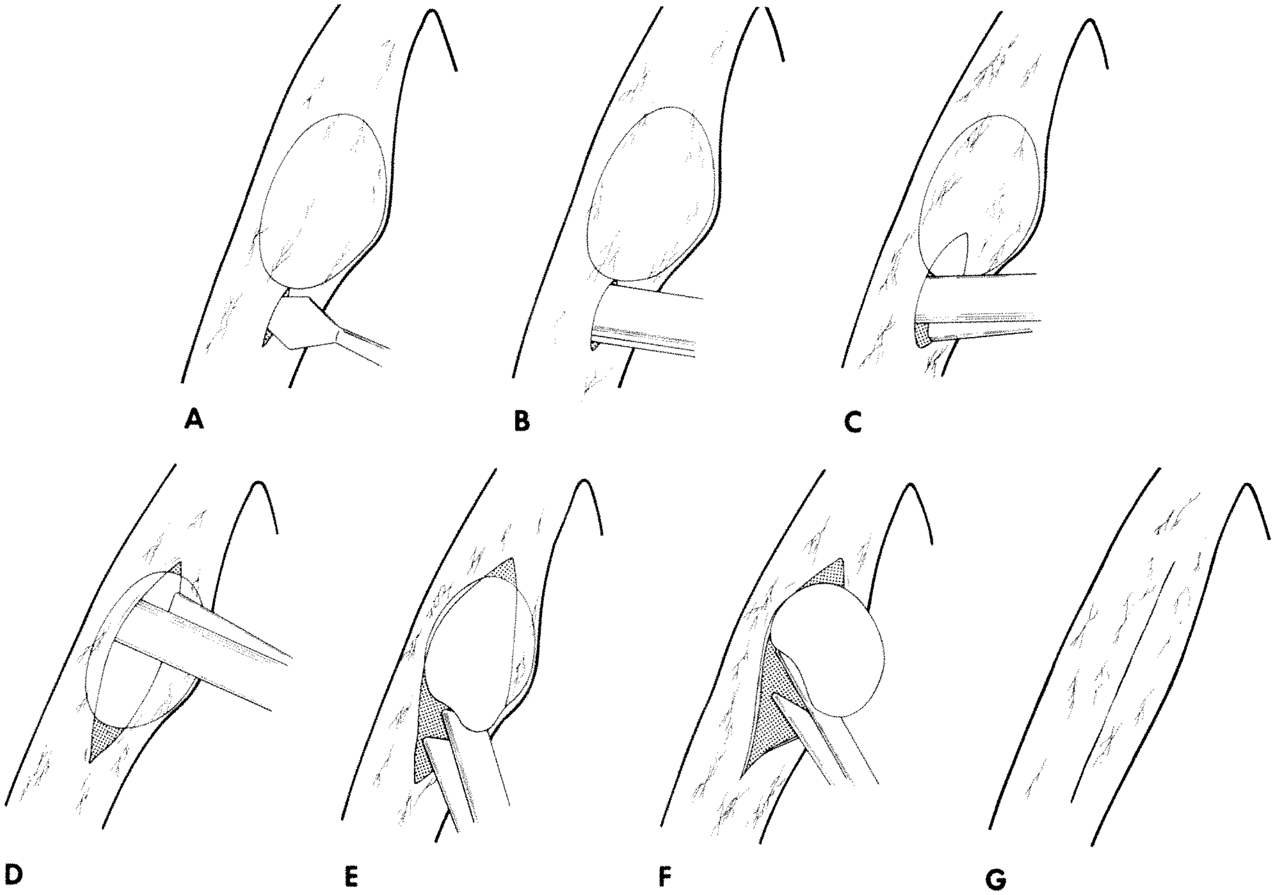

Fig 2. Schematic presentation of surgical technique. A) Incision. B) Insertion of elevator. C) Opening of elevator. D) Extension of incision anterior to cyst. E,F) Elevation of cyst from surrounding tissue. G) Single incision line remaining on upper aspect of vocal fold.

al incision over the cyst (Fig 2C). The procedure with the double-bladed elevator is repeated anteriorly until the incision is extended anterior to the cyst (Fig 2D). The cystic wall thus is totally exposed at the superior aspect. The cyst then is elevated very carefully from the neighboring tissue (Fig 2E,F).

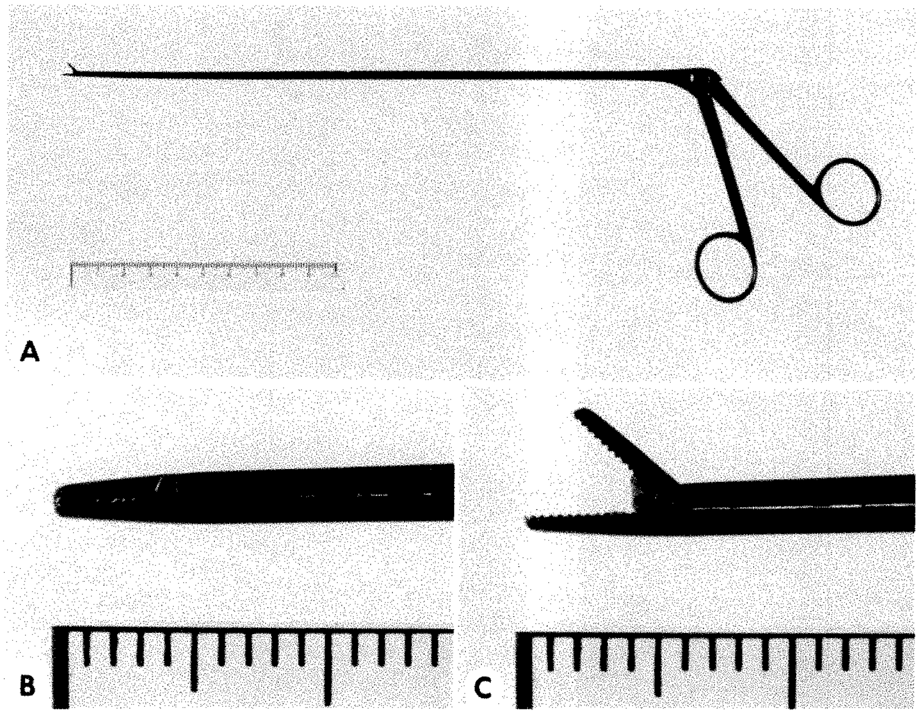

Fig 3. Double-bladed elevator. Rulers are in centimeters. A) Entire view. B) View of tip with blades closed. C) View of tip with blades opened.

TABLE 1. PATIENT DATA

Patient	*Age*	*Sex*	*Affected Side*	*Occupation*	*Vocal Use*	*Concomitant Disorders*
1	30	F	Left	Singer	Singing professionally	None
2	64	M	Right	Farmer	Singing as hobby	Reinke's edema
3	25	F	Bilateral	Kindergarten teacher	Singing in choir, talking frequently	None
4	42	F	Right	Supervising seamstress	Talking in noise	Sulcus vocalis, vocal nodule
5	44	M	Bilateral	Repairman	Singing as hobby	Sulcus vocalis
6	26	F	Bilateral	Kindergarten teacher	Talking frequently	None
7	52	M	Right	Driving teacher	Talking frequently, singing as hobby	None
8	40	F	Bilateral	Beautician	Talking moderately	None

The specially designed double-bladed elevator, a traditional single-bladed elevator, and a small piece of cotton are used most frequently for the elevation procedure. When the cyst is elevated from the surrounding tissue, it is taken out. A single incision line on the upper aspect of the vocal fold should be the result (Fig 2G).

Some cysts are connected to a sulcus vocalis (Fig 1B). In such case, the cyst is detached from the sulcus by a gentle pull of the cyst or by sectioning with scissors. Some cysts partly enter the vocal ligament (Fig 1C). The careful elevation procedure described earlier usually can elevate the cyst from the vocal ligament. The use of scissors occasionally is required. In any case, the surgery should be conducted carefully and scrupulously.

REVIEW OF CASES AND FUNCTIONAL RESULTS

During the period from April 1987 to June 1988, we operated on eight patients with the present technique (Table 1). Of the eight patients, three were men and five were women. Their ages ranged from 25 to 64 years. Four patients had a unilateral lesion, whereas the other four had bilateral lesions. Most patients were frequent voice users. Two patients had concomitant sulcus vocalis.

The vocal function was evaluated before and after surgery. The postoperative evaluation was conducted 6 months or more following surgery. The tests employed were perceptual evaluation of hoarseness[1]; stroboscopy[1]; measurement of maximum phonation time, mean airflow rate, lowest and highest physiologic tones, fundamental frequency range of phonation, softest and loudest tones, and sound pressure level range of phonation[1]; and acoustic analysis of voice.[2,3] In the acoustic analysis, pitch perturbation quotient, amplitude perturbation quotient, and normalized noise energy for 0 to 4 kHz and that for 1 to 4 kHz were determined for a sustained vowel /e/ produced at the habitual fundamental frequency and sound pressure level ranges of phonation.

The results of perceptual evaluation are shown in Table 2. All patients had had a mild to moderate degree of hoarseness preoperatively. Following surgery, five patients recovered normal clear voice, and three had a decrease in degree of hoarseness. Of the latter three, one (patient 4 in Table 1) had bilateral sulcus vocalis that could not be treated surgically. The other two (patients 6 and 7 in Table 1) continued to abuse their voices following surgery.

Preoperative laryngeal stroboscopy showed lack of mucosal wave over the cyst in all cases. A recovery of mucosal wave was noted postoperatively with every patient. The grade of mucosal wave varied, however. There was a tendency that the larger the cyst, the smaller the postoperative mucosal wave.

Preoperative and postoperative maximum phonation time, mean airflow rate, lowest and highest physiologic tones, fundamental frequency range, softest and loudest tones, and sound pressure level range are shown in Fig 4. Following surgery, maximum phonation time, highest physiologic tone, fundamental frequency range, loudest tone, and sound pressure level range tended to increase, and mean airflow rate was apt to decrease. Neither lowest physiologic tone nor softest tone differed markedly between the preoperative and postoperative conditions.

The results of acoustic analysis are shown in Fig 5. Pitch perturbation quotient, amplitude perturbation quotient, and normalized noise energy for 0 to 4 kHz and for 1 to 4 kHz decreased postoperatively in most patients, indicating an improvement in voice quality.

COMMENTS

An epidermoid cyst of the vocal fold is not a rare

TABLE 2. RESULTS OF PERCEPTUAL EVALUATION OF HOARSENESS (NO. OF PATIENTS)

	Preoperative				
	None	*Mild*	*Moderate*	*Severe*	*Total*
Postoperative					
None		2	3		5
Mild			3		3
Moderate					0
Severe					0
Total	0	2	6	0	8

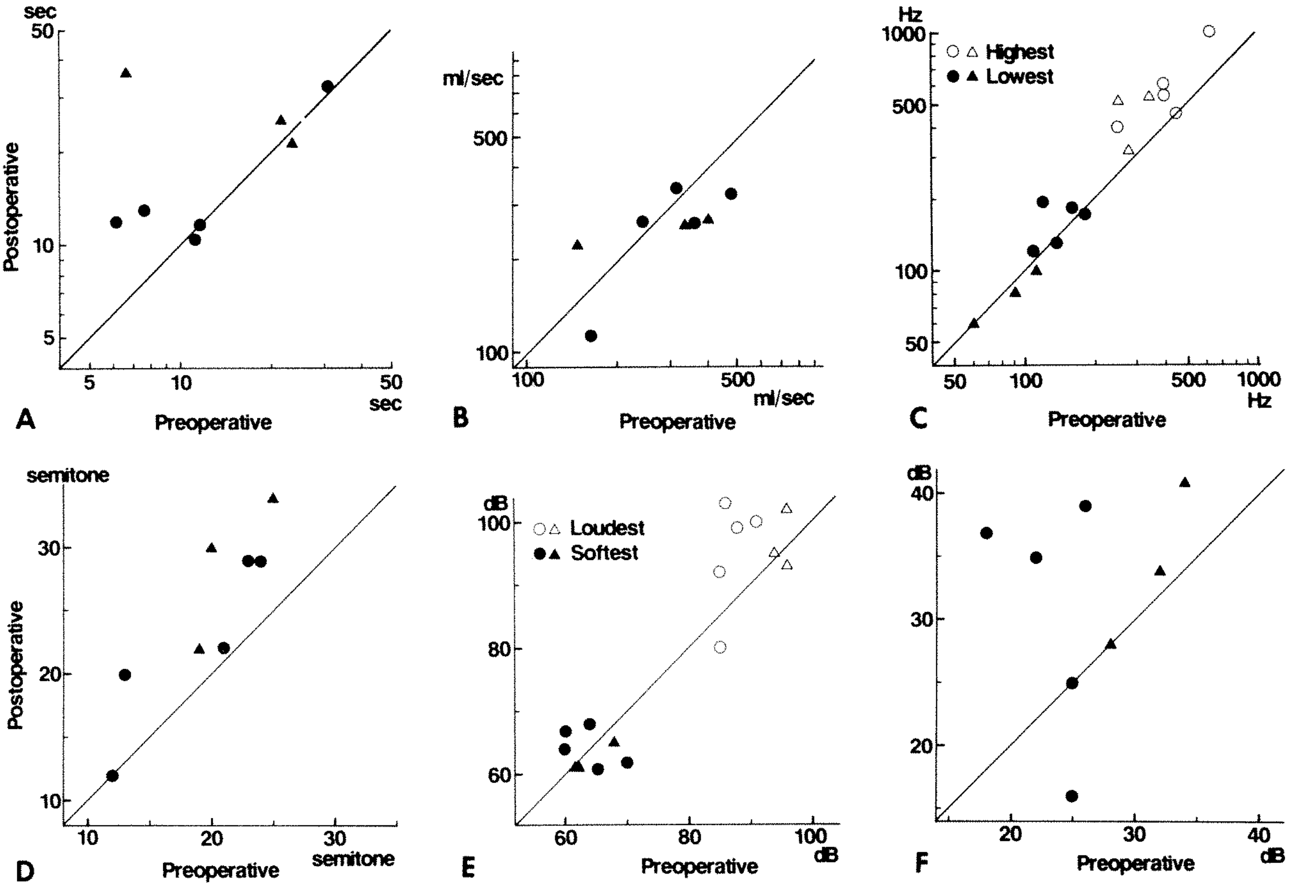

Fig 4. Preoperative and postoperative vocal function. Triangle — man, circle — woman. A) Maximum phonation time. Significantly increased in four patients. B) Mean airflow rate. Significantly decreased in five patients. C) Lowest and highest physiologic tones. Former did not change markedly in most patients, whereas latter was raised significantly in most patients. D) Fundamental frequency range of phonation. Significantly raised in most patients. E) Softest and loudest tones. Former did not show systematic changes, whereas latter was increased in five patients. F) Sound pressure level range of phonation. Increased in five patients.

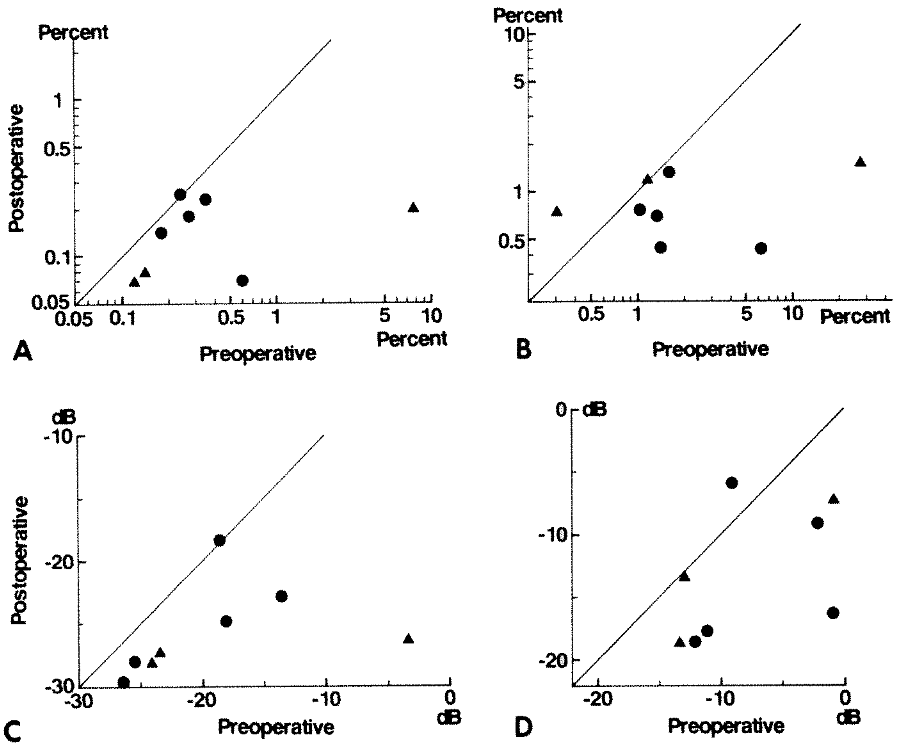

Fig 5. Preoperative and postoperative results of acoustic analysis. In most patients, all four measures were decreased significantly. Triangle — man, circle — woman. A) Pitch perturbation quotient. B) Amplitude perturbation quotient. C) Normalized noise energy for 0 to 4 kHz. D) Normalized noise energy for 1 to 4 kHz.

condition.[4] Fiberscopic and telescopic laryngeal stroboscopy has contributed greatly to our ability to detect small cysts that often are overlooked under traditional laryngeal mirror examination.

Surgical removal is the only existing modality to eradicate epidermoid cysts. Cysts basically are located in Reinke's space, which is a very pliable structure and is essential to normal vocal fold vibration.[5,6] Any procedure that causes scar formation should be avoided. A complete removal of the cyst with minimal surgical intervention in the neighboring normal tissue cannot always be conducted successfully.

The technique presented in this paper seems to be one of the best possible procedures for epidermoid cysts of the vocal fold. Compared to the technique in which an incision is made lateral to the cyst,[7] the medial wall of the cyst is elevated easily with the present method.

We are not able to compare the functional results of the present technique with those of other methods, since there have been no reports in which postoperative vocal function is described in detail. Comparison of postoperative vocal function among different surgical techniques awaits further study.

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PAN AMERICAN ASSOCIATION OF OTORHINOLARYNGOLOGY-HEAD AND NECK SURGERY

The XXII Congress of the Pan American Association of Otorhinolaryngology–Head and Neck Surgery will be held November 23-27, 1990, in Catagena, Colombia. For further information, contact Pedro Blanco, President, Pan American Congress, Hospital Universitario del Valle, 3er Piso Servicio de Otorrinolaringologia, Cali, Colombia.

Ann Otol Rhinol Laryngol 98:1989

REGIONAL BLOOD FLOW TO THE CANINE VOCAL FOLD AT REST AND DURING PHONATION

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Recent reports have suggested that blood flow to the vocal fold decreases during phonation. However, these studies relied on indirect measures of blood flow, such as tissue oxygen tension. Among the differing methods of measuring blood flow, one of the most sensitive is the microsphere surface technique. This technique has been effective in assessing the overall and regional blood flow to a number of different organs, including the cochlea. Employing an in vivo canine model, we injected microspheres into the left atrium. From there, they were distributed and became entrapped in the tissues in proportion to blood flow. We measured the blood flow to the entire vocal fold, as well as the lamina propria and muscularis layers. The results revealed a statistically significant ($p < .002$) increase in blood flow on phonation. The increase, however, was due to increased flow to the muscularis layer. The flow to the lamina propria remained unchanged during phonation.

KEY WORDS — blood flow, canine vocal fold, phonation.

INTRODUCTION

The microvascular anatomy of the vocal fold has been well described in humans and canines.[1,2] However, less is known about the actual blood flow to the larynx. Several reports using oxygen tension as an estimate of blood flow have suggested that during phonation, ischemic changes occur in the lamina propria and muscularis layers of the vocal fold.[3-5] Although it is controversial, some authors also have proposed that circulatory and ischemic changes are responsible for vocal fold polyps and nodules.[3,4,6-8]

In this study, the microsphere surface technique was used to measure the blood flow to the canine vocal fold in vivo, during rest and phonation.[9,10] This method also afforded the opportunity to measure the regional distribution of blood flow to the lamina propria and muscularis layers.

BACKGROUND

In 1967, a method for measuring blood flow using radioactive microspheres was introduced.[11] Radiolabeled carbon-coated microspheres were injected into the left atrium. From there, they were dispersed throughout the body in proportion to regional blood flow. Because the microspheres (10 to 15 μm diameter) were slightly larger than RBCs, they became entrapped in the tissue capillaries. Blood flow was calculated from the radioactivity of the tissue compared to a reference sample drawn from an arterial source. This method has been used extensively to evaluate the regional blood flow to organs such as the heart, kidney, pancreas, and recently the cochlea.[12-15]

The sensitivity of this method has been well documented and is related to the total number of spheres trapped in the tissue.[12] For example, Buckberg et al[14] were able to assess the effects of various physiologic conditions and medical regimens on coronary blood flow.

Other, less direct methods have been developed for measuring blood flow to an organ. These include clearance of hydrogen or xenon gas, laser-Doppler velocimetry, and diffusible radiolabeled tracers.[12,16-18] In a study that compared the sensitivity of some of these techniques in determining blood flow to the small bowel, the microsphere technique was found to be very reliable and served as the standard by which the other methods were compared. The hydrogen clearance method tended to overestimate the total blood flow. Laser-Doppler velocimetry showed good correlation with the microsphere blood flow; however, difficulties were encountered in relation to the depth of the tissue being measured and velocimetry resolution in thin tissue sections.[19] Tissue oxygen tension has been used as an indicator of blood flow, but it is actually a reflection of both arterial oxygenation and blood flow.[2]

Recently, the microsphere technique has been modified for use without radiolabeling. The blood flow is measured by counting the number of spheres in histologic sections (microsphere surface technique).[13,20-23] Although a laborious process, there

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Presented at the meeting of the American Laryngological Association, San Francisco, April 1-2, 1989.

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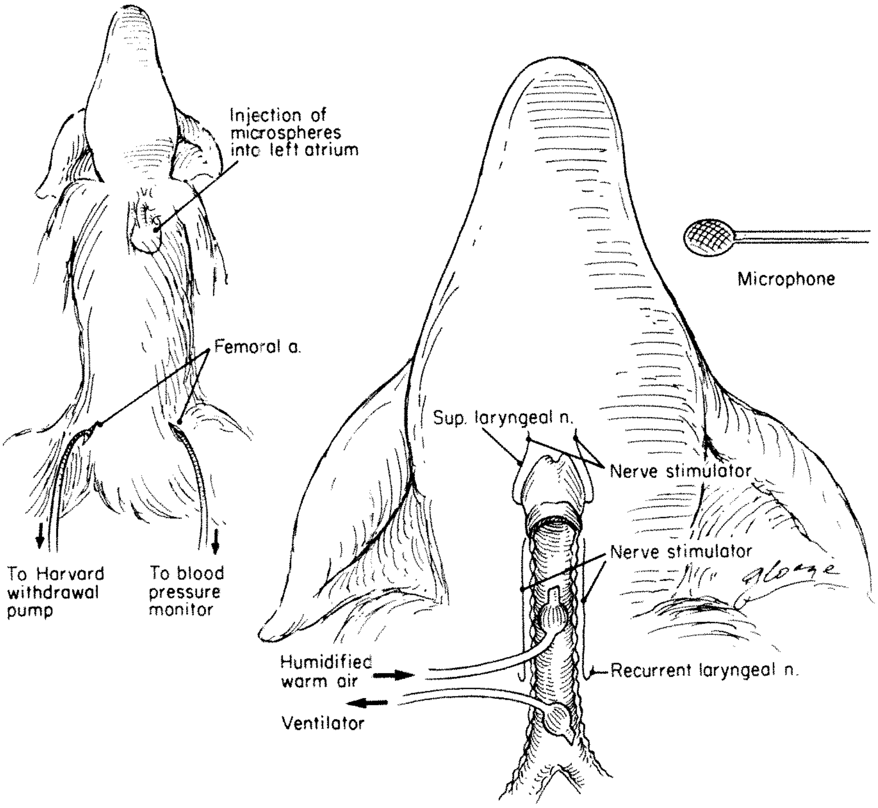

Fig 1. Experimental set-up.

are a number of advantages to this method. Blood flow can be measured to regions of an organ that could not be separated easily for counting of radioactivity (ie, flow to lamina propria versus muscularis layers). Also, the risks and expense of working with radioactive materials are avoided.

METHODS

In Vivo Preparation. Eight adult male mongrel dogs, weighing from 15 to 23 kg, were sedated with Innovar (Pitman-Moore, NJ) intramuscularly (1 mL/10 kg body weight). Sodium pentothal was administered intravenously to a level of corneal sensation loss, and this level of anesthesia was maintained with additional doses as required. The animal was placed supine on the operating table and orotracheally intubated (Fig 1). Respiration was maintained with a Bird ventilator. Catheterization of both iliac arteries was performed. The right iliac artery was connected to a Gaeltec pressure transducer (model DEC-1, Medical Measurements, Hackensack, NJ) to monitor blood pressure and pulse. The left side was connected to a Harvard withdrawal pump (Millis, Mass) for sampling of arterial blood during the procedure.

The body temperature of the animal was maintained at 37°C to 37.5°C throughout the experiment with heat lamps. A midline neck incision was made to expose the trachea, the larynx, and both superior and recurrent laryngeal nerves. The vascular supply to these structures and the investing fascia of the larynx and trachea was preserved. A low tracheostomy was performed at the level of the suprasternal notch, and an endotracheal tube was placed for ventilation after withdrawal of the orotracheal tube.

A second tracheostomy was performed in a more proximal location, and a cuffed endotracheal tube placed in a cephalad direction with the tip 10 cm below the vocal cords. The cuff was inflated to seal the trachea, and humidified air was passed through this tube with flow controlled by a flowmeter (Gilmont Instruments). The air was warmed to 37°C and humidified by being bubbled through 5 cm of heated water.

Through a midline sternotomy, a Silastic catheter was placed in the left atrium. The catheter was brought out through the superior portion of the wound, and the chest was closed.

The recurrent laryngeal nerves were isolated 5 cm below the larynx, and Harvard bipolar miniature electrodes were applied. The superior laryngeal nerves were isolated just proximal to their entry into the larynx, and electrodes were applied in a similar fashion. Two nerve stimulators (WPT Instruments, Quincy, Mass) with direct current isolation units were used to stimulate the recurrent and superior laryngeal nerves independently. These nerves were stimulated at 90 Hz at 2 to 9 mA with 1.5-ms pulses. Phonation was produced at an airflow of 318 mL/s supplied through the laryngeal ap-

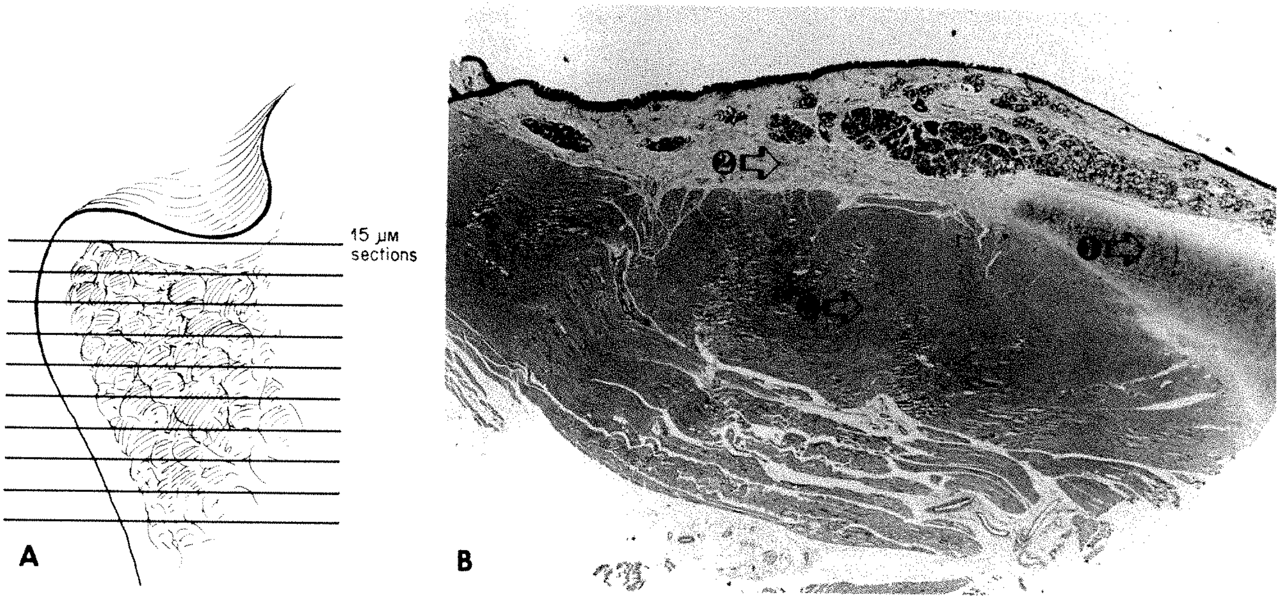

Fig 2. Sectioning of vocal fold. A) Schematic of sections. B) Representative vocal fold section. 1 — arytenoid cartilage, 2 — lamina propria, 3 — muscularis.

erture by the rostrally placed endotracheal tube during stimulation of the laryngeal nerves.[9,10] Analysis of the phonatory pitch was obtained from the frequency output of a Storz laryngostroboscope (model 8000).

Microsphere Injection and Withdrawal. Fifteen-micron microspheres (3M, St Paul, Minn) were used. They were suspended in 0.9 N saline with a trace of Tween 80. The microspheres were kept in suspension by ultrasonic agitation.

The number of spheres injected was determined from a preliminary study on five animals. The goal was to obtain sufficient spheres in the tissue sections to reduce counting and statistical errors without altering hemodynamics. The minimum number of spheres per injection was determined by the requirement that under the lowest blood flow conditions the resulting mean number of spheres per histologic section had to be at least two standard deviations above zero (assuming a normal distribution in the number of spheres trapped per histologic section). However, when too many spheres were injected, the small distal vessels became occluded and a true representation of flow was not obtained. Injection of 1.12 x 10^7 spheres/kg body weight resulted in the entrapment of approximately 20 spheres/section in the control group, with no apparent effects on the distribution or hemodynamic parameters. The preliminary studies also demonstrated that 99% of the microspheres were entrapped within the first 60 seconds. No microspheres were detected in the venous circulation, indicating that arteriovenous shunting was minimal.

Blood pressure, pulse, and temperature were monitored at 5-minute intervals and remained stable for at least 10 minutes prior to and during the experiment. The reference blood flow specimen was withdrawn at a rate of 7.75 mL/min for 90 seconds with a Harvard pump via the iliac artery. Withdrawal was initiated 15 seconds prior to injection. The 10-mL microsphere suspension was injected into the left atrium over a 5-second period, followed with a 10-mL flush of 0.9 N saline. No changes in vital signs were noted during or following any of the injections.

Experimental Design. The control group of four animals had microspheres injected without laryngeal nerve stimulation but with warm humidified airflow through the laryngeal inlet. The experimental group of four animals was phonated for a period of 15 seconds prior to microsphere injection and for 60 seconds after injection. Phonation was elicited as follows. Input tracheal airflow was maintained at 318 mL/s. Electrical stimulation to the superior laryngeal nerves was adjusted to a low constant level of 2 mA. Current to the recurrent laryngeal nerves was increased until phonation ensued and was varied to provide a fundamental frequency of 100 to 150 Hz. One additional unilateral experiment was performed with only the right superior and recurrent laryngeal nerves stimulated at 1 and 3 mA, respectively. In this case, no phonation was achieved when only one side was stimulated.

Blood Flow Calculation. After completion of the reference withdrawal, the animals were killed painlessly with an intracardiac injection of Eutha-6. The larynx was removed, and the vocal folds were removed carefully and placed in 10% formalin. For the purpose of this study, the vocal fold was defined as that portion of mucosa and muscularis extending from the arytenoid to the anterior commissure. The specimen was embedded in a paraffin block after

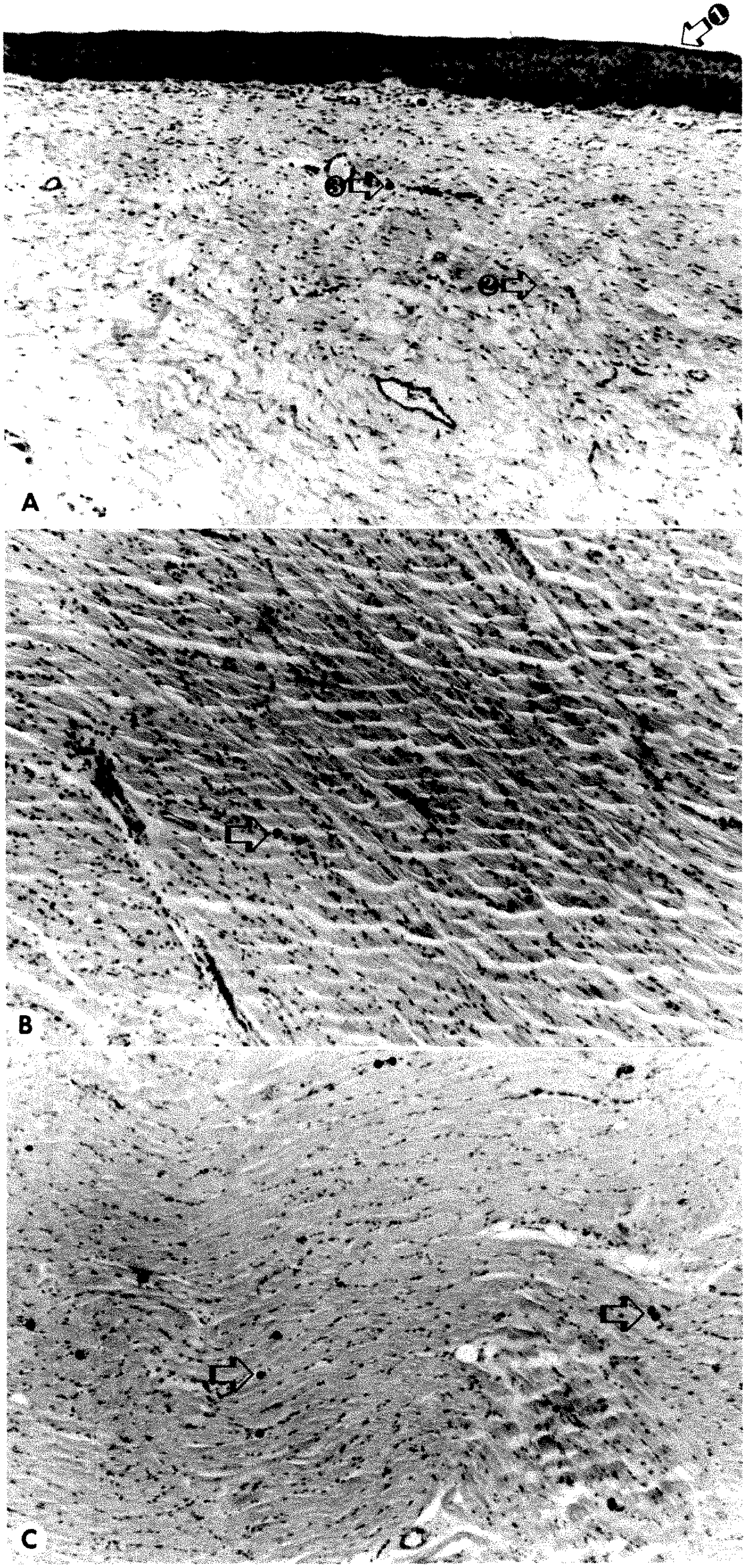

Fig 3. Distribution of microspheres. A) Lamina propria. 1 — mucosal layer, 2 — lamina propria, 3 — microsphere. B) Muscularis at rest. Arrow — microsphere. C) Muscularis during phonation. Arrows — microspheres.

CUMULATIVE DATA (BLOOD FLOW IN MILLILITERS PER MINUTE)

Subject	*Lamina Propria*	*Muscularis*	*Total*
Control (resting)			
1	3.62	8.18	11.80
2	6.01	5.00	10.01
3	6.95	5.44	12.39
4	6.19	7.10	13.26
Mean ± SD	5.44 ± 1.45	6.43 ± 1.48	11.87 ± 1.37
Experimental (phonation)			
1	4.48	45.78	50.14
2	6.74	74.02	80.76
3	5.78	51.18	57.46
4	5.75	91.14	96.90
Mean ± SD	5.69 ± 0.93	65.53 ± 21.01	71.32 ± 21.48
Unilateral stimulation			
Unstimulated	4.79	6.97	
Stimulated	5.39	66.26	

careful measurement of the width. Then it was sectioned in a longitudinal fashion (anterior to posterior; Fig 2). A stratified sampling procedure was used by taking ten equally spaced 15-μm sections. The sections underwent hematoxylin and eosin staining with metanil yellow counterstain. The slides were viewed under a light microscope, and the microspheres were visualized and counted easily. The numbers of spheres in the muscularis and lamina propria layers were counted separately. To find the total number of spheres in the vocal fold, the average number of spheres per section was multiplied by the number of possible sections in the fold based on its postpreparation measurement.

The reference blood samples were hemolyzed and then digested in 25% potassium hydroxide; then the spheres were recovered by centrifugation and counted with a hemacytometer. Blood flow was calculated from the following formula:

$$U_v = (S_v/S_t) \times U_k$$

where U_v = blood flow in the vocal fold, S_v = number of spheres in the vocal fold, S_t = total spheres in the reference sample, and U_k = reference blood flow (7.75 mL/min).

RESULTS

The microspheres appeared well distributed throughout the vocal fold. There were occasional small vessels seen that were occluded by a group of spheres, but the majority of spheres were distributed individually (Fig 3).

Mean blood flow to the vocal fold at rest and during phonation is depicted in the Table and Fig 4. Total flow as well as regional flow to the muscularis and lamina propria is depicted. Total blood flow increased from 11.87 mL/min at rest to 71.32 mL/min during phonation. However, the increase in flow was entirely due to the increase in flow to the muscularis layer, with even distribution throughout the layer. The flow to the lamina propria was unchanged during phonation, and no gross change in distribution was noted.

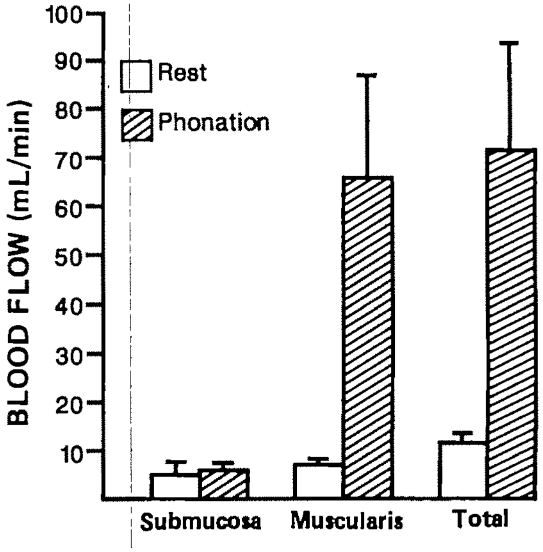

Fig 4. Mean blood flow and standard deviation at rest and during phonation.

In the statistical analysis of the data, a two-way factorial design with one repeated measure was employed. The between-subject factor was phonation (resting versus phonating). The within-subject variable was location (lamina propria versus muscularis). The dependent measure was blood flow, which was calculated as shown above. The blood flow was markedly increased on phonation: F(1,6) = 30.19 ($p < .002$). There was a significant interaction, demonstrating that the increase in flow between the resting and phonating states was the result of the increase in flow exclusively to the muscularis: F(1,6) = 32.43 ($p < .001$). In post hoc testing, there was no difference between rest and phonation in flow to the lamina propria (Newman-Keuls, $p < .001$).

In the unilateral experiment, electrical stimulation of the right side did not elicit phonation, but the blood flow to the right lamina propria and muscularis mirrored that in the phonating animals (5.39 and 66.26 mL/min, respectively). In contrast, the left, nonstimulated side's blood flow was the same as that of the control group (4.79 and 6.97 mL/min, respectively).

DISCUSSION

The microvascular anatomy described by Hirano[1,2] may explain why the blood flow to the lamina propria and muscularis can change independently during phonation. The blood vessels in the free edge portion of the lamina propria run longitudinally and arise from the anterior and posterior ends of the vocal fold, having no contact with the underlying muscularis layer. The vessels in the muscularis run upward and medially from deep inside the layer.

During phonation, the lamina propria receives a constant blood supply despite the underlying muscular contraction with its greatly increased blood supply. It is quite a remarkable system that allows the lamina propria to vibrate in such a rapid fashion without affecting blood flow.

When the recurrent and superior laryngeal nerves were stimulated on one side only, the blood flow in the muscularis layer of the stimulated side was the same as that in the phonating subjects. The blood flow to the muscularis of the nonstimulated vocal fold was the same as that in the resting vocal fold. This suggests that the increased flow during phonation was caused by muscular contraction and not vocal fold vibration.

The finding that blood flow rises in the vocal fold during phonation is contrary to the findings of Matsuo et al[4] and Hiroto et al.[3] Using oxygen tension (Po2) as an estimate of blood flow, Matsuo et al found a slight decrease in Po2 in the lamina propria and a large decrease in the muscularis during phonation. As discussed, the difficulty with using oxygen tension as an estimate of blood flow is that it is a reflection of both blood flow and arterial oxygenation. Oxygenation is dependent on many variables, including metabolic activity, ie, muscle contraction. Thus, the decline in oxygen tension may reflect only the increased oxygen consumption, rather than a change in blood flow. Other problems with their studies[3,4,6] include the following: the method required an implanted or contact electrode that altered the normal vibratory pattern of the vocal fold; the electrode also may have altered flow because of its physical presence in or on the tissue; one of the experimental designs relied on painful stimuli to elicit phonation, which also invoked a strong sympathetic response probably affecting blood flow.

The microsphere technique offers the advantages of a truly in vivo method of accurately assessing regional blood flow. The disadvantages are that it requires killing the animal and that the surface technique is not practical in the analysis of blood flow in large organs.

CONCLUSIONS

Study of the blood flow to the vocal fold in an in vivo canine model demonstrated a rise in flow during phonation. This increase was due to increased flow to the muscularis layer. No significant change in the flow to the lamina propria was observed. The rise in blood flow to the muscularis resulted from muscular contraction and not vibration of the vocal folds.

There were no ischemic changes in the vocal folds during 90 seconds of phonation. Thus, there was no evidence to support the theory that ischemic changes regularly occur during phonation and are etiologically associated with the formation of vocal nodules or polyps. Further study is required to assess whether ischemic changes might occur after repeated episodes of prolonged phonation.

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The Casselberry Award was established to encourage the advancement of the art and science of laryngology and rhinology. The award is given for outstanding theses or accomplishments in laryngology and rhinology and consists of a suitable sum of money and a certificate from the Association. Competition for this award is limited to those persons whose abstracts are selected for consideration for inclusion in the annual scientific program. Abstract forms may be obtained from the Secretary, H. Bryan Neel, MD, 200 First Street SW, Rochester, MN 55905. Individuals wishing to compete for this award must submit an entry in the form of a complete thesis to Eugene N. Myers, MD, President, 230 Lothrop Street, Pittsburgh, PA 15213, no later than December 1, 1989. The candidates and theses will be reviewed by a committee. If a winner is selected, the Casselberry Award will be presented at the 111th annual scientific meeting, to be held at the Breakers Hotel in Palm Beach, Florida, April 28-29, 1990.

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LONG-TERM RESULTS OF SACCULOTOMY IN OLDER PATIENTS

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In patients with Meniere's disease with incapacitating vertiginous complaints in whom medical treatment has failed, sacculotomies by both the Fick and tack operations are relatively simple surgical procedures, whose short duration of anesthesia and hospitalization of patients minimizes the risks of morbidity in older patients appropriately to their general health, with good results in controlling vertigo. With respect to preservation of hearing, the tack operation is superior to the Fick operation.

KEY WORDS — Meniere's disease, older patients, sacculotomy.

INTRODUCTION

Meniere's disease can be controlled by medical treatment in approximately 70% to 75% of patients.[1,2] However, when medical treatment has failed to control vertigo and/or progressive inner ear hearing loss, surgical treatment is to be considered.[2] Surgical procedures can be either conservative, aimed at preservation of hearing and comprising operations on the endolymphatic sac and the vestibular nerve, or radical, aimed at destroying the labyrinth. Long-term results of conservative procedures showed successful control of vertigo in 49% to 81% of shunting procedures of the saccus, depending on the technique used, and in 95% and more of vestibular nerve sections; but in many cases eventual deterioration of hearing is observed.[1-5] Although vestibular nerve section produces excellent results in controlling vertigo, it carries considerable potential morbidity.[1] A comparatively innocuous alternative to this major surgical procedure is sacculotomy, as described by Fick in 1964[6] and modified by Cody et al,[7] who described the tack operation in 1967. This paper discusses long-term results on vertigo and hearing of these procedures.

MATERIAL AND METHODS

Thirty-nine patients diagnosed as having classic Meniere's disease were operated on by the second author (G.D.L.S.) during the period between 1965 and 1976. A Fick operation was performed on 19 patients in the period between 1965 and 1968, and 20 patients underwent a tack operation in the period between 1967 and 1976. Two Fick patients and one tack patient failed follow-up and are excluded from the report. The average age of patients in the Fick group was 54 years (range, 29 to 87 years) and in the tack group 52 years (range, 36 to 72 years). Ten patients in the Fick group and six patients in the tack group were male. In total, seven patients eventually developed bilateral Meniere's disease (three in the Fick group and four in the tack group).

The average duration of symptoms prior to surgery was 5 years in the Fick group (range, 1 to 11 years) and 6 years in the tack group (range, 1 to 16 years). Three patients in the Fick group and six patients in the tack group had a speech discrimination score of 0% preoperatively in the involved ear. Thus, preoperatively serviceable hearing in the involved ear existed in 14 of the Fick patients and 13 of the tack patients.

In sacculotomy by means of the Fick operation a small tympanomeatal flap is elevated to provide access to the oval window. The center of the stapes footplate is punctured with a needle to a depth of 2 mm, the fenestra thus created is covered with Gelfoam, and the tympanomeatal flap is replaced. In the modification of this operation by Cody et al,[7] a stainless steel tack is inserted through the footplate immediately behind the base of the anterior crus after exposure of the oval window region in the same way as in the Fick procedure. Gelfoam is put in the oval window niche, and the tympanomeatal flap is replaced.

The mean follow-up of the Fick patients was 17 years 10 months (range, 1 year 5 months to 23 years 8 months) and of the tack patients 12 years 1 month (range, 3 years to 19 years 7 months). All patients still living were followed up for the maximum possible period. Data on results were obtained from the patients' postoperative history concerning vertigo and hearing, and the objective assessment of the patients' hearing by means of pure tone audiograms (0.5, 1, 2, and 4 kHz) and speech discrimination tests obtained in the postoperative period. The results were reported in accordance with the guidelines established in 1972 by the American Academy of Ophthalmology and Otolaryngology (AAOO; Table 1).[8] In determining hearing results a com-

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Presented at the meeting of the American Otological Society, Inc, San Francisco, April 2-3, 1989.

TABLE 1. AAOO CRITERIA FOR REPORTING RESULTS IN TREATMENT OF MENIERE'S DISEASE

Class	*Criteria*
A	Vertigo relieved; hearing improved (15 dB speech reception threshold or 15% speech discrimination gain)
B	Vertigo relieved; hearing unchanged
C	Vertigo relieved; hearing deteriorated (15 dB speech reception threshold or 15% speech discrimination loss)
D	Vertigo not relieved

Information from reference 8.

AAOO — American Academy of Ophthalmology and Otolaryngology.

parison was made between the best preoperative audiogram and the most recent postoperative audiogram.

RESULTS

Overall, 82% of the patients in the Fick group had satisfactory control of their vertigo, and in the tack group this was 89%. The remainder had no satisfactory improvement in vertigo, requiring labyrinthectomy in three of the Fick group (18%) and in two of the tack group (11%). This is shown in Table 2.

In both groups, when no preoperative aidable hearing existed in the involved ear, vertigo control was 100%. In ears with preoperative aidable hearing, vertigo was controlled in 79% in the Fick operations and 85% in the tack operations. No relationship was found between failure to control vertigo and patient age.

The results according to the AAOO classification system are summarized in Table 3.[8]

Hearing improved postoperatively in two patients (12%) in the Fick group. One patient (5%) in the tack group showed postoperative hearing improvement. Hearing stayed the same (within 15-dB limits) in 6% of the Fick and 42% of the tack ears. Deterioration of hearing (more than 15 dB) was found in 64% of the Fick patients and 42% of the tack patients. In the Fick group 14 had preoperative aidable hearing. Postoperatively this was preserved in only five. In the tack group, of 13 patients with preoperative serviceable hearing, three developed anacusis postoperatively. Thus, hearing was preserved in 36% in the Fick operations and in 77% in the tack procedures.

It is important to note that signs of contralateral hydrops, shown in a 15-dB or more hearing loss or a 15% or more speech discrimination loss, developed eventually in 25% of all the patients in these two groups.

TABLE 2. OVERALL VERTIGO CONTROL

	Satisfactory		*Unsatisfactory*	
	No.	*%*	*No.*	*%*
Fick (n = 17)*	14	82	3	18
Tack (n = 19)*	17	89	2	11

*Of 19 patients undergoing Fick operation, two failed follow-up and are not included. Of 20 tack patients, one failed follow-up and is not included.

TABLE 3. RESULTS ACCORDING TO AAOO CLASSIFICATION

	*Fick (n = 17)**		*Tack (n = 19)**	
Class	*No.*	*%*	*No.*	*%*
A	2	12	1	5
B	1	6	8	42
C	11	64	8	42
D	3	18	2	11

Classification from reference 8.

AAOO — American Academy of Ophthalmology and Otolaryngology.

*Of 19 patients undergoing Fick operation, two failed follow-up and are not included. Of 20 tack patients, one failed follow-up and is not included.

The Figure shows the bivariate distributions of results of Fick and tack procedures on the hearing in the operated and the contralateral ear.

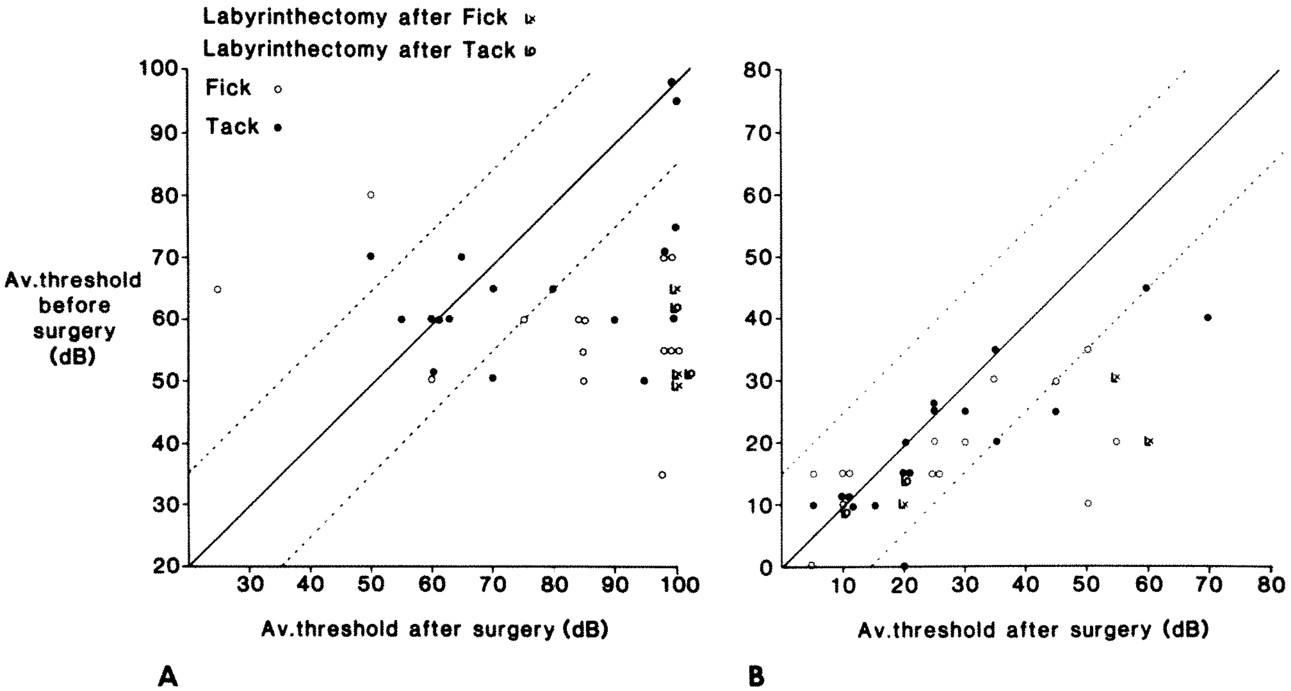
DISCUSSION

Surgical treatment in Meniere's disease is aimed primarily at control of incapacitating vertigo. Preservation of hearing, however, is also an important aim, because of the possible involvement of the contralateral ear at a later stage resulting in severe auditory incapacity. As a consequence, it is widely felt that destructive procedures are contraindicated in ears with aidable hearing, although one recent report claimed that the risk of severe hearing impairment in the uninvolved ear is not great.[9]

A variety of operations on the endolymphatic sac have been performed since Portmann[10] first suggested its drainage to achieve relief of vertigo. Most of these procedures were aimed at decompressing the sac by means of shunting the endolymph to other tissues or compartments, such as the subarachnoid space[11] or the mastoid cavity, by means of various methods[12-16] and showed successful control of vertigo in 49% to 81%.

In this period, sacculotomy as described by Fick and Cody was introduced. The first results of the Fick procedure were published in 1964 in a report dealing with 50 patients with a mean postoperative follow-up period of 2 years 8 months, showing an overall relief of vertigo in 76% of the cases while hearing deteriorated in only 4%.[6] Results of the tack operation were reported first in 1968 in 57 patients[17] and later in 1983, when results in two series of patients with a mean postoperative follow-up period of 12 years 9 months and 9 years 4 months, respectively, showed a 79% satisfactory control of vertigo in both groups, while hearing was maintained or improved in 60% to 66% of the patients.[18]

Reports on results of vestibular nerve section show control of vertigo in 95% and more of the cases,[1,5,19] but apart from the fact that this procedure requires exceptional degrees of skill and special training for the surgeon, morbidity may be consid-



Bivariate distribution of final hearing status in A) operated ear and B) contralateral (nonoperated) ear.

erable, and long-term results show that hearing deteriorates in many cases.[4,20,21] Therefore, suitability of the Meniere's patient over 50 years of age is questionable.

Our results of the sacculotomy procedures show an overall relief of vertiginous symptoms in 82% of the patients who had a Fick procedure and in 89% of those treated with a tack procedure. Preservation of hearing was achieved in 36% of the patients in the Fick group and 77% of those in the tack group. Nine patients (53%) with preoperative serviceable hearing developed a dead ear after the Fick operation, whereas only three (16%) developed a dead ear after the tack procedure. In our experience, sacculotomy has great value in the conservative surgical management of Meniere's disease for older patients with good contralateral hearing who are incapacitated by vertigo. The overall results of the tack procedure are numerically superior to those of the Fick operation with respect to preservation of hearing and control of vertigo. The tack procedure is a relatively innocuous operation and is an attractive alternative to saccus decompression and vestibular nerve section in older or debilitated patients with stable contralateral hearing.

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CALL FOR PAPERS
SECOND INTERNATIONAL COCHLEAR IMPLANT SYMPOSIUM

The University of Iowa Department of Otolaryngology–Head and Neck Surgery and the International Cochlear Implant Association will hold the Second International Cochlear Implant Symposium in Iowa City on June 4-9, 1990. The symposium will focus on basic science aspects of electrical stimulation on the auditory system, new cochlear implant strategies, clinical application in both adults and children, and rehabilitation and educational issues. Please submit abstracts to Bruce J. Gantz, MD, Department of Otolaryngology–Head and Neck Surgery, University of Iowa Hospitals and Clinics, Iowa City, IA 52242.

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TREACHER COLLINS SYNDROME: AN OTOLOGIC CHALLENGE

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Patients with Treacher Collins syndrome have severe middle ear malformations that render operation difficult. We have evaluated 43 patients with Treacher Collins syndrome, on whom only 11 were operated. Computed tomography, the single most important study done preoperatively, routinely showed an underdeveloped temporal bone with islands of bone marrow and absent mastoid pneumatization. The middle ear space was often underdeveloped. Ossicular dysjunction was often noted in which the fused malleus/incus remnant was found 3 to 4 mm distant to the stapes. A common finding was severe dysplasia of the stapes–facial nerve complex that often made the middle ear malformation uncorrectable. Hearing results were much less predictable than in patients with isolated atresia/stenosis of the ear.

KEY WORDS — craniofacial disorders, middle ear malformations, Treacher Collins syndrome.

INTRODUCTION

Treacher Collins syndrome (mandibulofacial dysostosis) is an autosomal dominant genetic disorder having full penetrance and variable expressivity. The fully expressed phenotype will show characteristic dysmorphic features involving the face, eyes, mandible, and ears. Specifically, there is an antimongoloid slant to the palpebral fissures, colobomata of the lower lids, a depressed malar region, retrognathia, and usually malformed pinnae. The syndrome becomes progressively more severe in succeeding generations and may become lethal.[1] However, genetic counseling has assumed a more prominent role, and the familial pattern of the syndrome has decreased. Most cases seen today are mutations.

Otologists long have recognized that surgery for hearing is difficult in patients with Treacher Collins syndrome. The middle ear is often small, sometimes being represented only by a small bony cleft. The malleus and incus are often absent, and when present usually are fused. The stapes arch, if present, is characteristically monopodal, being represented by a single crus. The oval window is smaller, being about half the normal size. The facial nerve frequently is displaced and bare throughout its middle ear course. The tympanic membrane is of normal size only in those patients showing very mild expression of the phenotype. Even when the tympanic membrane is normal in appearance, the stapes–facial nerve axis may be severely malformed.

The net effect of the deranged middle ear architecture is to make surgery for hearing rehabilitation very difficult, if not impossible. Patients with Treacher Collins syndrome should never be surgically "tested" by the novice otologist. Even experienced otologists find it a difficult task, and while some may elect to operate, none can claim good results consistently.

This manuscript will attempt to define those Treacher Collins patients who may qualify as surgical candidates on the basis of the appearance of the middle ear as studied by high resolution computed tomographic scanning. Unlike patients with isolated nonsyndromic microtia and aural atresia, Treacher Collins patients are never routinely "good candidates." However, before consigning this group of patients to a lifetime of amplification by virtue of a device, implantable or not, we believe that in carefully selected patients it is appropriate that an attempt be made to provide hearing through surgery in at least one ear.

METHODS AND MATERIALS

Computed Tomography. Forty-three patients with Treacher Collins syndrome were evaluated over a period of 15 years. Twenty-one patients were seen subsequent to 1982, when we began the routine use

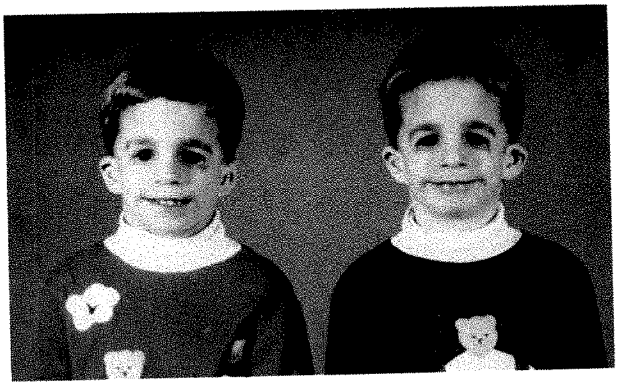

Fig 1. Monozygotic twins with Treacher Collins syndrome.

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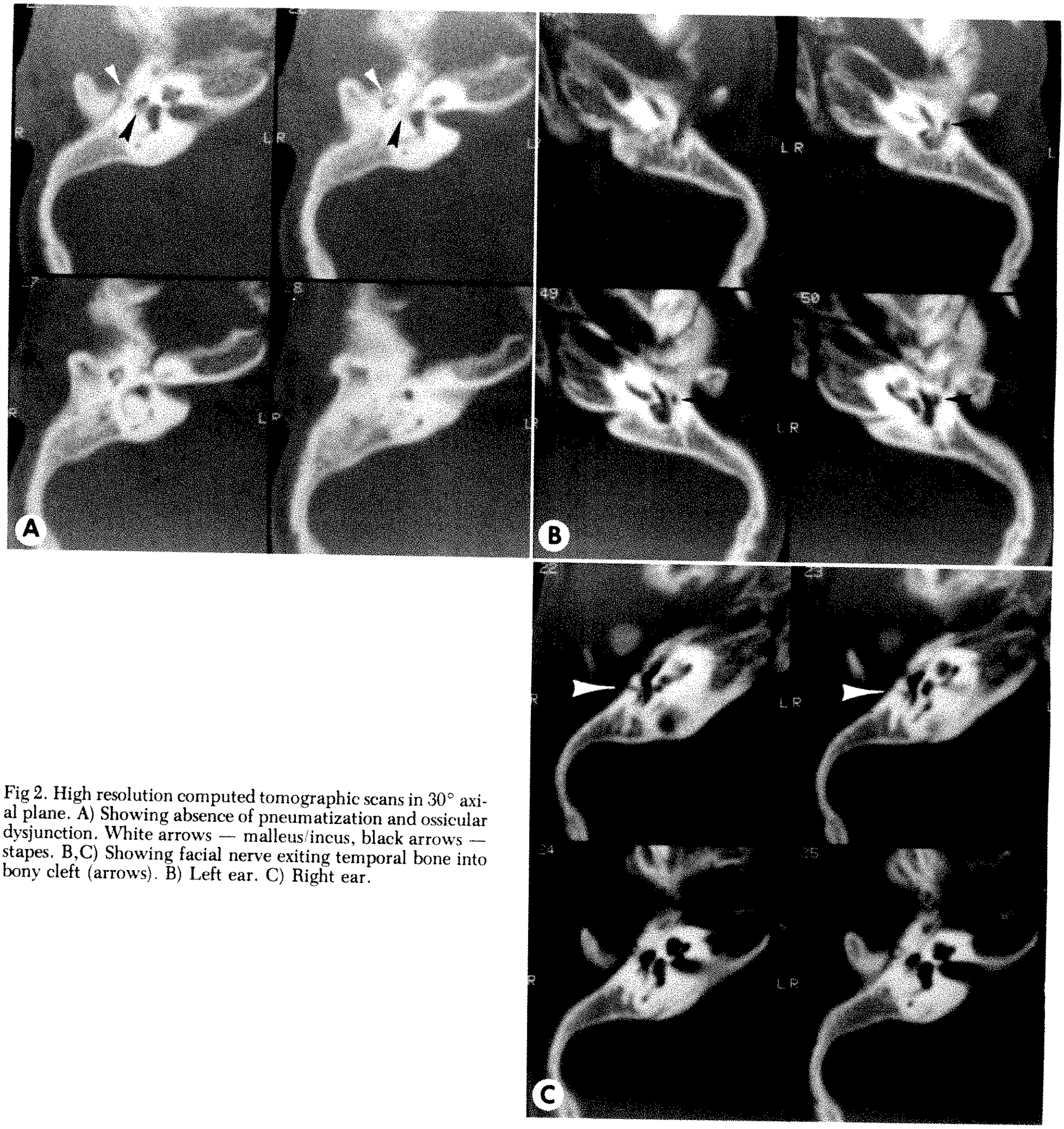

Fig 2. High resolution computed tomographic scans in 30° axial plane. A) Showing absence of pneumatization and ossicular dysjunction. White arrows — malleus/incus, black arrows — stapes. B,C) Showing facial nerve exiting temporal bone into bony cleft (arrows). B) Left ear. C) Right ear.

of high resolution CT scanning of the temporal bones. Sixteen of these 21 patients were scanned.

Scanning was performed with a GE 9800 scanner in the 30° axial and 105° coronal planes. Contiguous 1.5-mm slices at 1.0-mm intervals were taken with a 0.5-mm overlap to better detail minute structures within the temporal bone. Images were reconstructed from the raw data with a standard GE bone algorithm program and were displayed and photographed with an extended window. Life-size images were produced by use of the 512 matrix, a display field of view of 12.8, the specific x and y coordinates, the multiple display photographic format, and a large image size on the filming device. It is important to emphasize that simple magnification techniques may not be used, as detail will be lost.

Magnetic resonance imaging was not performed routinely, as this method of study does not image bone. More recently, we have begun to include three-dimensional reconstructions of the CT scan to better define the temporal bone anomaly as seen on the lateral aspect of the skull.

Surgery. Eleven of 43 patients were operated upon. Nine patients had surgery in an attempt to improve hearing, while two other patients were operated upon for otologic disease: one patient had a perforated tympanic membrane with cholesteatoma, and the other patient had a chronic infection

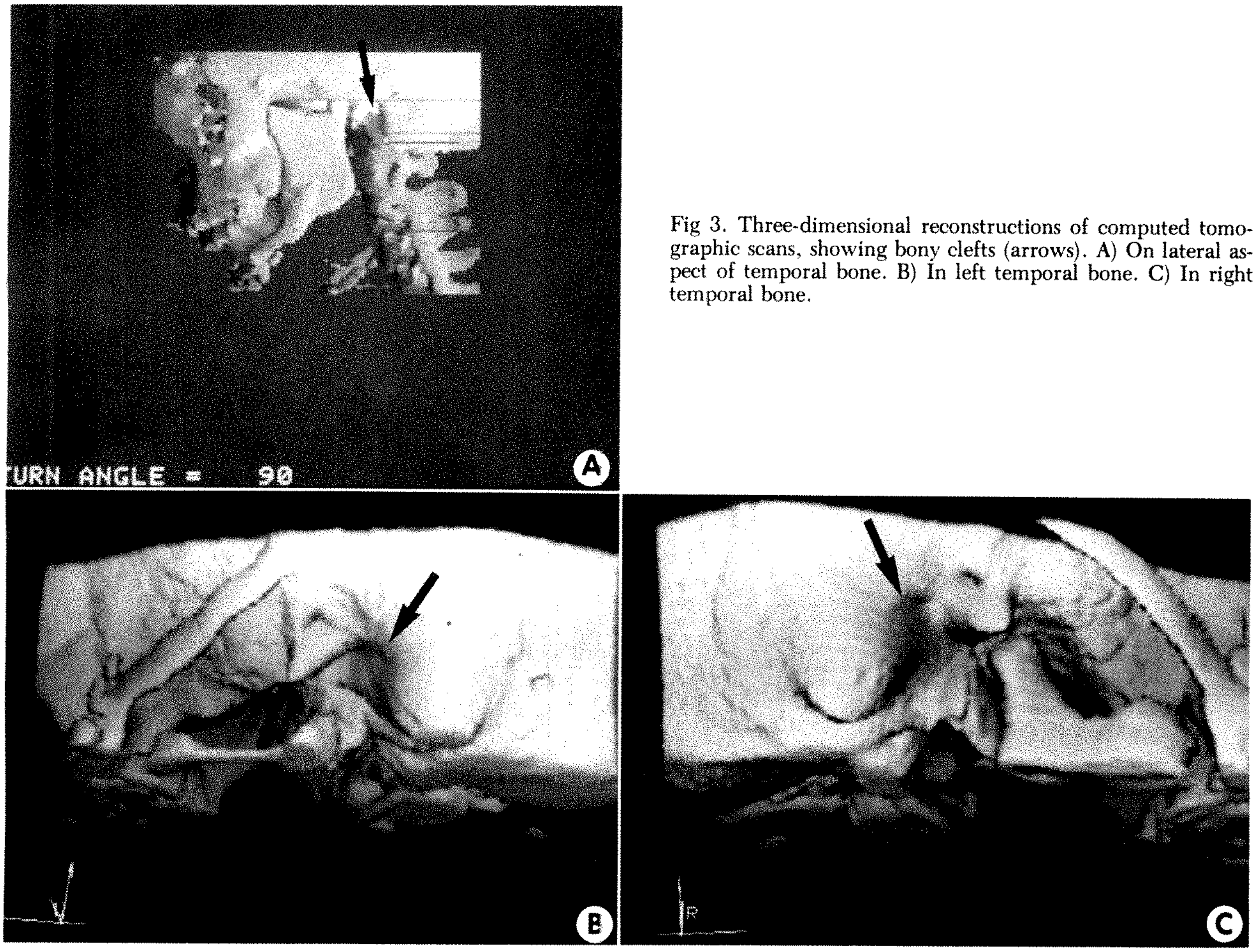

Fig 3. Three-dimensional reconstructions of computed tomographic scans, showing bony clefts (arrows). A) On lateral aspect of temporal bone. B) In left temporal bone. C) In right temporal bone.

of the middle ear. The youngest patient in the surgery group was 4½ years, while the oldest was 57 years. There were seven males and four females. Two of the males were monozygotic twins (Fig 1). Four of the 11 patients had complete atresia of the ear canal, four had stenosis with a small tympanic membrane, and three had a tympanic membrane that was only slightly malformed. All patients had a bilateral conductive hearing loss on preoperative audiologic testing.

Of the 11 surgical patients, the phenotypic expression was complete in two and incomplete in nine. Of the incomplete group, five were considered to have mild cases.

RESULTS

Computed Tomography. There were three radiographic findings noted on CT scanning that made the Treacher Collins group unique and separated them from nonsyndromic patients with microtia and aural atresia. First, there was absence of mastoid pneumatization. In no patient with this syndrome was the mastoid bone found to be pneumatized. There were various degrees of aeration of the middle ear cleft, sometimes extending to the antrum, but never involving the mastoid bone. Second, there was ossicular dysjunction. The fused and malformed malleus/incus complex was found to be 3 to 4 mm distant from the stapes (Fig 2A) bilaterally in four patients and unilaterally in two patients. Only three patients in whom ossicles could be identified failed to show this separation. Nine patients had partial or complete absence of ossicles, either bilaterally or unilaterally. The third finding was a commonly seen bony cleft in the lateral aspect of the temporal bone just anterior to the mastoid. This cleft was confirmed by three-dimensional reconstruction of the CT scan (Fig 3A).

Surgery. Surgery was straightforward in only two patients. One young boy with a moderate conductive hearing loss, a malleus handle with an abnormal curve anteriorly, and an absent stapedial reflex was found to have thick secretions in the middle ear space. The secretions were evacuated, the middle ear was ventilated, and hearing was improved to normal thresholds. The second straightforward case involved a teenage girl in whom there was a congenital absence of the incus long process. An interposed incus strut restored hearing to normal thresholds.

Two patients were not primarily operated on for hearing rehabilitation. One, a 57-year-old man with a tympanic membrane perforation and cholesteatoma, was found to have a congenital absence of

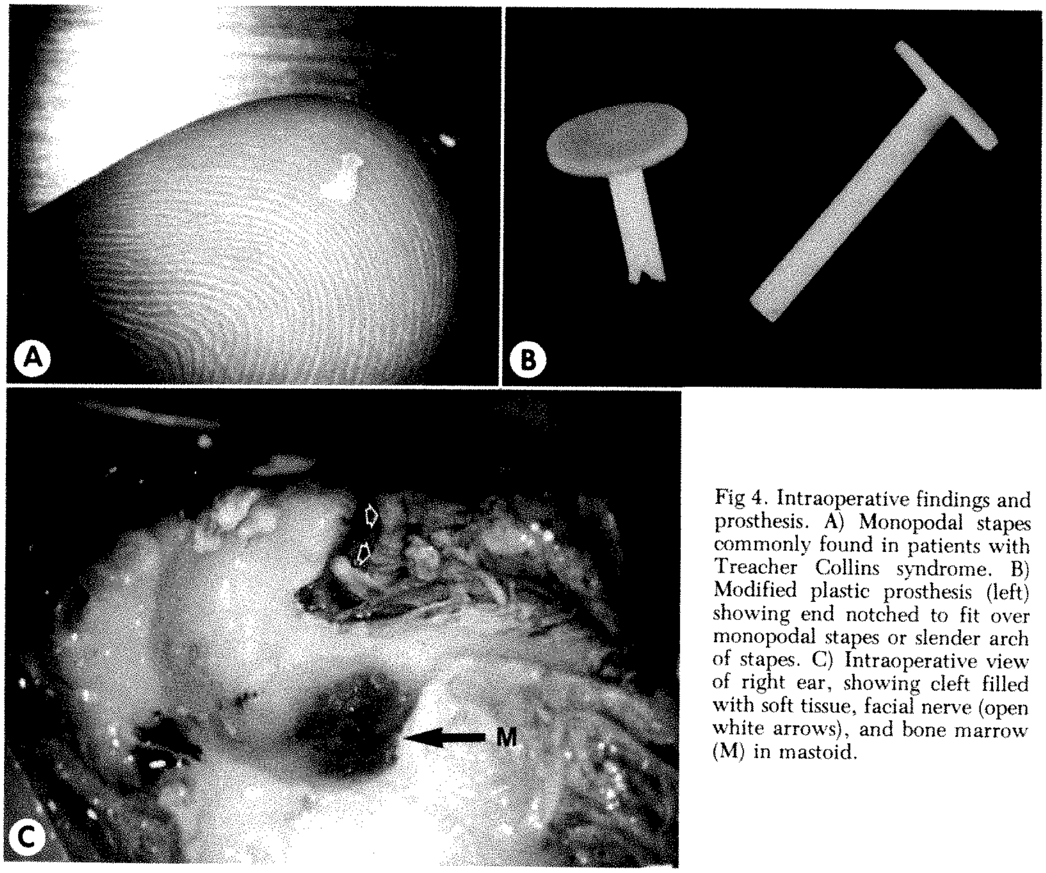

Fig 4. Intraoperative findings and prosthesis. A) Monopodal stapes commonly found in patients with Treacher Collins syndrome. B) Modified plastic prosthesis (left) showing end notched to fit over monopodal stapes or slender arch of stapes. C) Intraoperative view of right ear, showing cleft filled with soft tissue, facial nerve (open white arrows), and bone marrow (M) in mastoid.

the stapes and oval window, and a bare facial nerve over the promontory. A second patient, a 12-year-old boy, had chronic otitis media with a small perforation and multiple loculations in the middle ear that contained purulent secretions.

Surgery in the remaining seven patients was difficult. One patient with complete atresia was operated on early in the series, prior to the advent of CT scanning. A middle ear was not found. A fenestration of a semicircular canal was performed with no improvement in hearing. It was impossible to determine if the semicircular canal being fenestrated was the lateral or superior canal. A severe malformation of the skull base and an anatomic rotation of the bony labyrinth within the temporal bone precluded accurate identification. With the temporal bone imaging of today, this patient would not qualify as a surgical candidate.

Ossicles. Ten of 11 patients had a malformation of the malleus/incus complex. The malleus and incus were fused in six patients, absent in one patient, and not found in the patient with no identifiable middle ear. One patient had a congenital absence of the incus long process, and another had an anterior-curving malleus handle.

Eight of 11 patients had an abnormal stapes. Five stapes were monopodal (Fig 4A), two were small and malformed, and in one patient the stapes was absent. Additionally, the stapes was not found in one patient. In two patients the stapes was normal.

Facial Nerve. The middle ear segment of the facial nerve was bare and displaced in five patients, bare and nondisplaced in one patient, partially bare in another patient, bifid in one patient, and not found in one patient. In two patients the facial nerve had a normal middle ear course and appearance.

Oval Window. The oval window was smaller than normal in six patients, normal in three patients, absent in one patient, and not found in the patient with no middle ear. Of six patients with a small oval window, three had a footplate obscured by a bare facial nerve (Fig 5). One other patient had congenital fixation of the stapes footplate.

Surgical Repair. Middle ear reconstruction in this patient group demanded the best effort and talent of the surgeon. In seven patients with atresia or stenosis, a canalplasty and tympanic membrane reconstruction was performed simultaneously with the ossicular chain repair. There was often dysjunction of the malleus/incus and the stapes. Not infrequently, a fused malleus/incus complex was located 3 to 4 mm distant to the oval window. This separation of the ossicles had been noted previously by Phelps et al.[2,3] The net effect of this separation was to render the malleus/incus unusable for a stapes prosthesis or incus replacement prosthesis. Our procedure of choice was to modify a synthetic flanged

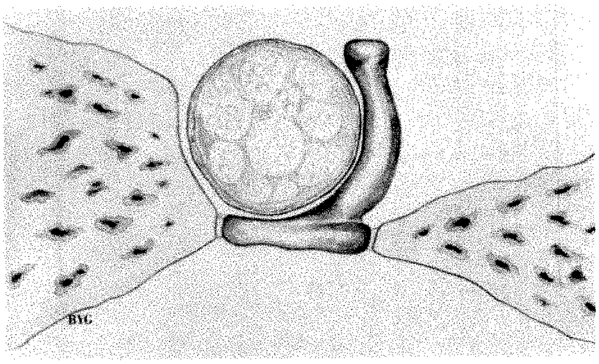

Fig 5. Illustration of coronal view through right ear, showing bare facial nerve covering oval window. Note deformed stapes.

prosthesis and place the shaft over the stapes (Fig 4B). Frequently, the stapes was found to be monopodal or represented by a slender arch. In no case was there a well-formed stapes head and neck. A commercial partial ossicular replacement prosthesis was not feasible, as this was found to weigh too heavily on the stapes arch. It was necessary to use a lightweight plastic prosthesis to avoid stapes necrosis.

Hearing Results. The hearing results were much less satisfactory in this group of patients than in patients with isolated congenital aural atresia (see Table). Only in three patients were normal thresholds achieved that endured long-term. Two other patients had normal postoperative hearing (20 dB) short-term that later regressed. In three patients there was no change.

DISCUSSION

High resolution CT scanning of the temporal bones is the single most important study done in the preoperative assessment of patients with Treacher Collins syndrome. It not only will determine if the patient is a candidate for surgery, but may also influence intraoperative decisions. Preoperatively, the size of the middle ear cleft, the presence or absence of ossicles, the patency of the labyrinthine windows, and the course of the facial nerve are pieces of information gleaned from the CT scan that are essential in making a decision to operate. On the other hand, absence of mastoid pneumatization, ossicular dysjunction, and the presence of a bony cleft will warn the surgeon to expect a degree of difficulty not usually encountered in routine atresia repair.

Lack of mastoid pneumatization does not mean that one is dealing simply with a sclerotic mastoid. In Treacher Collins syndrome patients, the mastoid bone is laced with islands of bone marrow that tend to bleed throughout the entire surgical procedure. Absence of pneumatization also means that there are no air cell tracts to guide the surgeon: no pathways, no landmarks, just solid bone interspersed with marrow. In this milieu the specter of facial nerve injury is present and the bony labyrinth is at risk of accidental fenestration.

HEARING RESULTS (N = 11)

	Speech Reception Threshold (dB)	
Patient	*Preoperative*	*Postoperative*
1	60	20
2	60	35
3	60	60*
4	60	35*
5	60	55
6	55	35
7	45	20
8	30	15

There was no change in three other patients.

*Postoperative threshold was 20 dB short-term.

Ossicular dysjunction, a condition in which the malleus/incus complex is located distant to the stapes, is found in severe malformations of the temporal bones. This is a common finding in Treacher Collins syndrome patients and patients with hemifacial microsomia,[3] but is not routinely found in patients with isolated congenital atresia of the ear. The obvious implication of this ossicular separation is that the malleus/incus complex cannot be used to reconstruct the middle ear sound-conducting mechanism. Because the malleus/incus is not aligned with the stapes and oval window, an interposed incus strut is impractical and a stapes prosthesis would be useless.

To our knowledge, the finding of a lateral temporal bone cleft has not been reported previously. We have noted bony clefts at surgery, on CT scans, and more recently on three-dimensional reconstructions (Fig 3B,C). A bony cleft is noted in those patients with Treacher Collins syndrome who have complete ear canal atresia. The cleft is anterior to the mastoid and probably involves the squamous portion of the temporal bone in its inferior aspect at the level of the mandibular fossa. A tympanic bone remnant is an inconsistent finding and probably does not contribute to the cleft.

The clinical significance of the bony cleft stems from the fact that it is filled with soft tissue through which the facial nerve courses as it exits the temporal bone (Fig 2B,C). The facial nerve ascends laterally within the soft tissue of the cleft and may present at or near the lateral surface of the skull (Fig 4C). To be unaware of this anomaly is to court disaster, as dissection into the cleft may injure the facial nerve.

We also report for the first time the occurrence of Treacher Collins syndrome in monozygotic twins. Both members of the twin pair have been operated on, and identical middle ear findings were noted that involved a malformed stapes and a bare facial nerve covering the oval window. While the ossicular reconstructions were identical, the postoperative hearing results were not. One twin achieved a long-term speech reception threshold of 20 dB, while the other twin had a significant hearing improvement in the early postoperative period followed by sudden regression of the hearing to preoperative levels.

It is common to think of Treacher Collins syndrome as a genetic disorder with bilateral expression. While this is generally true of the soft tissues of the face, it is less true for the facial skeleton, base of skull, and temporal bones. Marsh et al[4] have studied the facial skeleton of 14 patients with Treacher Collins syndrome by three-dimensional surface reformation imaging from CT scans. They found that right-left asymmetry consistently characterized the bony deformities in all patients studied. They also noted that the most consistent skeletal aplasia involved the zygomatic process of the temporal bone and was present in 89% of patients studied. The external auditory canal was bilaterally absent in 43% of patients studied. Marsh et al[4] have pioneered the use of three-dimensional CT in the study of craniofacial abnormalities, including Treacher Collins syndrome. We plan to extend this imaging modality to our patients with congenital ear malformations to better define the problem.

Middle ear surgery remains a challenge, and few reconstructions are straightforward. Dealing with a small, delicate, underdeveloped stapes requires lightweight prostheses that can be modified intraoperatively to meet the needs of the patient. The facial nerve is often in the way and frequently needs to be displaced to determine the status of the stapes and oval window. In addition to the middle ear reconstruction, patients with stenosis/atresia require that a new tympanic membrane be constructed and an external ear canal created. Healing of the new tympanic membrane may place tension on the flange of the prosthesis and dislodge it from the stapes. For this reason, the patient or parents must be told beforehand that a second operation or a staged procedure may be necessary.

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SAN FRANCISCO OTOLOGY UPDATE: 1989

A course entitled San Francisco Otology Update: 1989, will be held November 2-4, 1989, at the Mark Hopkins Hotel in San Francisco. For further information, contact Extended Programs in Medical Education, University of California, Room U-569, San Francisco, CA 94143-0742; (415) 476-4151.

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COCHLEAR IMPLANT REVISION: EFFECTS OF REIMPLANTATION ON THE COCHLEA

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The removal of an indwelling cochlear implant electrode followed by reinsertion of a new device has been a maneuver of uncertain consequences to the cochlea and its surviving neural population. The present study was conducted in an attempt to elucidate the factors that determine whether a reimplantation procedure will be successful. Cochlear implantation followed by explantation and subsequent reimplantation was performed in eight adult cats. Evaluation of cochlear histopathology suggested a significant increase in electrode insertion trauma when there was proliferation of granulation tissue in the round window area and scala tympani. In other cases, atraumatic reinsertion was achieved without apparent injury to the cochlea. The results of a survey of cochlear implant manufacturers and surgeons indicate that electrode replacement can usually be accomplished without adverse effects. Difficulties have been encountered, however, in removing implants with protuberant electrodes and when reimplantation was attempted on a delayed basis following explantation.

KEY WORDS — cochlear implant, revision.

INTRODUCTION

During the 1980s, nearly 2,000 cochlear implant devices have been implanted worldwide. In coming decades this number undoubtedly will increase substantially, particularly when implantation of congenitally deaf children becomes widely practiced. It can be anticipated that the need for removal of indwelling cochlear implant electrodes followed by their replacement with new devices is likely to increase substantially in the future. A considerable number of contemporary and future cochlear implant systems will fail after years of continuous use. Prolonged contact with corrosive physiologic saline eventually may breach the hermetic insulating envelope that shields delicate electronic components. Also, microprocessors, diodes, and capacitors have finite life spans and are subject to eventual failure. The intracochlear electrode arrays themselves, although designed to be long lasting, probably will fail after decades of use.

One strategy for decreasing the frequency of reimplantation procedures is the utilization of an internal disconnect system that permits replacement of failed electronics or allows upgrading without disturbing the intracochlear electrode. Such systems were employed in a few early multichannel implant designs. However, they have been abandoned in current-generation devices because they were prone to failure.

Beyond these limitations to the life span of a particular cochlear implant device, the greatest potential limitation to the longevity of an indwelling cochlear implant is obsolescence. There can be little doubt that the future development of highly superior multichannel electrode arrays will raise the issue of risk versus benefit concerning the replacement of existing devices for upgrade purposes. Such considerations are especially critical to the implantation of deaf children, as device failures and compelling upgrades are a virtual certainty over a 70-year-plus life span.

MATERIALS AND METHODS

The study comprised two separate approaches to defining factors relevant to the success or failure of cochlear reimplantation. First, we conducted an experimental study in cats to delineate cochlear histopathologic consequences of implantation and replacement surgical procedures. In addition, we conducted a clinical survey to gather results available from experience with cochlear implant patients who have undergone reimplantation.

Devices and Experimental Protocol. The animal study was designed to evaluate two different types of reimplantation. Eight healthy young adult cats underwent bilateral cochlear implantation (Fig 1). In all cases, the right cochleas were implanted with a model long multichannel electrode consisting of a 7-mm-long silicone rubber cylinder. These ears served as once-implanted controls for comparison with the left cochleas, which underwent two implant procedures. The first experimental series evaluated replacement of a short single-channel implant with a long multichannel one. In four cats, the left

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From the Coleman and Epstein Laboratories, Department of Otolaryngology–Head & Neck Surgery, University of California, San Francisco. Supported in part by National Institutes of Health contracts NS-7-2391 and NS-3-2353. This study was performed in accordance with the PHS Policy on Humane Care and Use of Laboratory Animals, the NIH *Guide for the Care and Use of Laboratory Animals*, and the Animal Welfare Act (7 U.S.C. et seq.); the animal use protocol was approved by the Institutional Animal Care and Use Committee (IACUC) of the University of California, San Francisco.
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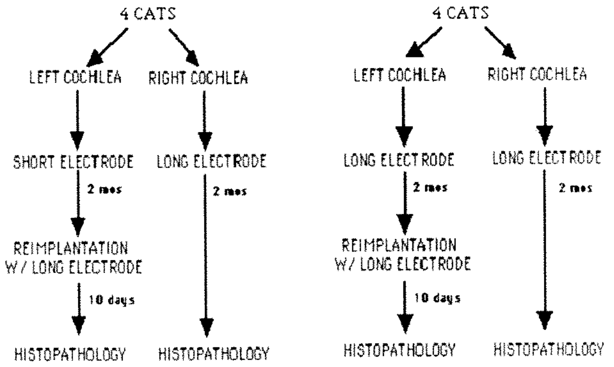

Fig 1. Experimental protocol for animal study.

ears initially received a model single-channel implant consisting of a wire (90% platinum, 10% iridium) with an apical ball that was inserted approximately 3 mm into the basal scala tympani. Two months later, this short implant was replaced with the 7-mm-long model multichannel electrode. The second experimental series evaluated replacement of an indwelling multichannel cochlear implant. In four animals, a long electrode was implanted in the left ear, and 2 months later the device was removed and replaced with an identical long electrode. As mentioned previously, the right ear in all eight animals was implanted with a model long electrode that remained undisturbed throughout the 2-month experimental period.

For all surgical procedures, animals were anesthetized with ketamine hydrochloride (30 mg/kg) and acepromazine maleate (0.3 mg/kg). After opening of the bulla, the round window membrane was incised sharply, and the electrode was threaded into the cochlea to the point at which resistance was felt. Ten days following replacement of the left implant, the animals were killed painlessly, and both cochleas were processed for histology. This relatively short survival period following reimplantation was chosen so that acute changes from the second procedure could be distinguished more readily from chronic pathologic changes due to the initial implant.

Histologic Preparation of Cochlear Specimens. At the time of death, animals were heavily anesthetized by intravenous administration of sodium pentobarbital, and cochleas were preserved in vivo by gentle perilymphatic perfusion of mixed aldehyde fixative (2.5% paraformaldehyde and 1.5% glutaraldehyde in 0.1 mol/L phosphate buffer at pH 7.4). The scala tympani electrode remained undisturbed within the scala tympani during the fixation procedure. A small opening was created in the cochlear apex by careful curettage. Then, the stapes was avulsed and the perfusion was carried out by careful infusion of fixative through the scala vestibuli via the oval window and the apical opening. Following transcardiac perfusion with the same fixative (with the addition of 4% sucrose), temporal bones were removed and postfixed for 24 hours. After thorough rinsing in buffer, the eighth nerve was dissected from the internal auditory meatus for separate processing, and the implanted electrode was withdrawn carefully from the fixed specimen under visual control. By use of diamond dental burs the cochlea was isolated, the otic capsule bone was thinned until the stria vascularis was clearly visible throughout the spiral, and several small openings were made into the scala vestibuli. The specimen then could be decalcified for a relatively short period (18 to 24 hours) in 0.1 mol/L EDTA. Next the cochlea was postfixed in phosphate-buffered osmium tetroxide, dehydrated gradually in ethanol, and embedded in Epon. The embedded cochlea was bisected on the midmodiolar plane. A few midmodiolar sections were cut; then a surface preparation was made. Each half-coil was removed, trimmed, and mounted in Epon on a glass slide. Complete reconstruction of the cochlear spiral was thus possible as 0.5-mm segments of the cochlea were selected for remounting and sectioning. The radial nerve fibers were clearly visible through the decalcified osseous spiral lamina and were used for orienting razor cuts so that radial sections of the organ of Corti and associated spiral ganglion could be cut in a single block. Semithin sections were cut at 1 to 2 μm, stained with toluidine blue, and coverslipped in immersion oil.

Clinical Survey. The clinical survey gathered data from manufacturers and implant teams involved in the placement of multichannel cochlear implants. Particular attention was directed to cochlear patency problems encountered during second electrode insertions and to significant deterioration in patient performance on post-reimplantation audiologic testing.

RESULTS

HISTOPATHOLOGY

Histopathologic results from the study are summarized in the Table. Because of the small number of specimens in each reimplantation category (four), these experimental results are best considered as individual case studies. However, three points should be noted from the Table. First, in both reimplantation series ("long to long" and "short to long"), there was one animal in which no neuronal loss was seen after the two implantation procedures and the observed pathologic changes were judged to indicate no additional hazard as a consequence of the two procedures. Second, every reimplantation case except one showed the presence of a middle ear effusion, whereas in the series with a single procedure, effusion was noted in only one case. This finding probably is related to the short postimplantation interval prior to evaluation in the reimplantation series. A third observation is a roughly twofold increase in traumatic insertion in the twice-operated cases. Difficulties with reinsertion in these,

HISTOPATHOLOGIC RESULTS

Cats	Middle Ear Effusion	Round Window Granulation Tissue	Scala Tympani Infection or Inflammation	Trauma	Organ of Corti Degeneration	Ganglion Cell Loss
Long electrode controls						
5207R	–	–	–	–	–	–
5364R	–	–	–	–	–	–
6073R	(Serous)	–	–	–	–	–
6046R	–	+ +	+	–	–	–
5456R	–	+ +	+	–	–	–
5522R	–	+	+	–	+ (B)	+ (B)
5454R	–	+ + +	+ + +	+	+ + (B,M)	+ (B,M)
5453R	–	+ + +	+	+ +	+ + + (B)	+ + + (B)
Reimplantation study (long to long)						
5522L	+ +	+ +	+	–	–	–
5364L	(Serous)	+ + +	+ +	–	+ +	–
6073L	–	+	+	+	+ (B)	+ + (B)
6046L	(Serous)	+ + +	+ + +	+ +	+ + (B)	+ + (B)
Reimplantation study (short to long)						
5207L	+	+	+	–	–	–
5453L	+ + +	+ +	+ +	–	–	+
5456L	+	+ +	+ +	+ +	+ +	+ +
5454L*	+ + +	+ + +	+ + +	+ + +	+ + + (B,M,A)	+ + + (B,M,A)

Minus sign indicates normal structure. Pluses indicate mild (+), moderate (+ +), or severe (+ + +) damage.

B — basal cochlear turn, M — middle cochlear turn, A — apical cochlear turn.

*Electrode was avulsed.

animals were associated with the proliferation of granulation tissue in the round window and scala tympani. That is, after removal of the initial implant, in those ears with marked granulation tissue in the round window area it was necessary to dissect away this tissue — a procedure often resulting in bleeding and awkward reimplantation.

In order to illustrate the range of pathologic changes across the experimental series, histologic findings from three ears will be presented in detail. The most severe pathologic changes were observed in a reimplantation animal in which a short electrode was replaced by a long array (Fig 2). During the second procedure, it was noted that the round window area and surrounding bulla exhibited prolific granulation tissue that had to be resected before reimplantation was possible. At the time of sacrifice, the electrode actually had been avulsed from its position in the scala tympani, presumably by the ingrowth of new granulation tissue. At operation, the tip of the replacement electrode had been inserted 5 mm into the scala tympani. In this case, the presence of an inflammatory exudate with numerous fibroblasts, polymorphonuclear leukocytes, monocytes, and lymphocytes in the middle ear and auditory bulla indicated acute otitis media. The round window membrane was markedly thickened with metaplasia of the epithelial layer to tall columnar-type respiratory epithelium with many ciliated and secretory cells. The middle layer was thickened and edematous with inflammatory cell infiltrate. The inflammatory process extended into the scala tympani and was accompanied by severe endolymphatic hydrops. Additionally, a rupture of the basilar membrane was observed in the basal hook region. All of these changes resulted in very significant loss of spiral ganglion neurons both adjacent to the implanted electrode in the basal turn and extending beyond the implant site to the middle and apical turns.

In another illustrative case (Fig 3), a model long electrode was replaced by an identical prosthesis. The second implantation procedure was noted by the surgeon to be difficult because of granulation tissue that encapsulated the original electrode and occluded the lumen of the scala tympani after explantation. Inflammatory response in the basal scala tympani and associated osteoneogenesis displaced the second electrode toward the modiolus. The implant clearly was not channeled into the identical site occupied by the first electrode. It should be noted that the difficult reimplantation in this case did not result in extensive damage to the spiral ganglion cell population, which appeared to be relatively normal throughout the cochlea. Degeneration of the organ of Corti was noted in the extreme basal aspect of this cochlea. However, at levels apical to the round window the basic cytoarchitecture of the tunnel of Corti was maintained and inner hair cells were present, although the outer hair cell region and space of Nuel appeared to be consolidated somewhat.

The final illustrated case exemplifies the more encouraging results from this reimplantation series (Fig 4). In this case a long electrode was implanted initially and replaced subsequently with another long device in the second operation. The round window membrane was thickened and edematous, but the scala tympani was relatively devoid of in-

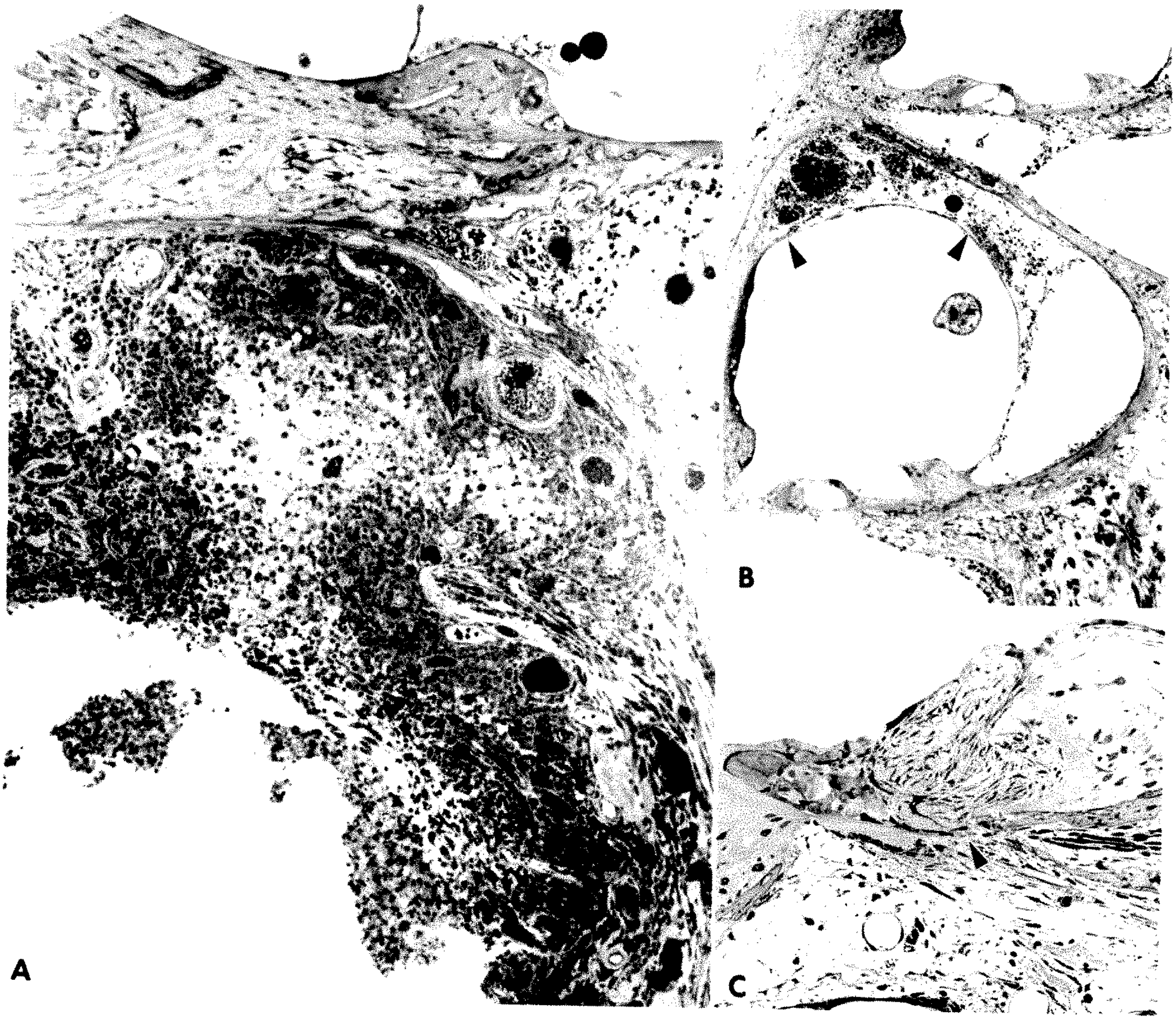

Fig 2. Severe pathologic changes in reimplantation case in which model short single-channel electrode was implanted initially, and subsequently replaced by model long multichannel electrode. A) Inflammatory reaction extends into scala tympani near round window, as shown in this radial section from basal cochlea. B) Endolymphatic hydrops as evidenced by distension of Reissner's membrane (arrowheads). Further, significant loss of spiral ganglion neurons is noted both adjacent to implanted electrode in basal turn (lower right of micrograph) and extending beyond implant site to middle and apical turns. C) Rupture of basilar membrane (arrowhead) in extreme basal or "hook" region.

flammatory cells, and the spiral ganglion cells appeared normal. Reactive fibrous connective tissue surrounded the implant, and the organ of Corti appeared relatively normal with recognizable hair cells, although the inner spiral bundle region under the inner hair cell was vacuolated. The minimal pathologic changes seen in this reimplanted case were equivalent to the most favorable results seen in the control series.

A final interesting observation within this series is that the use of absorbable gelatin sponge (Gelfoam) around the electrode near the round window membrane seemed to be correlated with the formation of excessive granulation tissue. Later cases in the series in which the use of Gelfoam was avoided appeared to give somewhat better results.

CLINICAL SURVEY

Each manufacturer of multichannel implants in the United States was queried regarding its experience with implant revision surgery during which the intracochlear electrode was replaced. Further details were obtained from numerous implant surgeons around the country who related their personal experience with cochlear reimplantation. The primary focus of this survey was to identify difficulties encountered during reinsertion of long multichannel electrodes into previously implanted cochleas. This priority was established because the great majority of future cochlear implants are anticipated to be of multichannel design. In some cases, the removed electrode was of the short single-channel type, while in others a long multichannel device was replaced.

Replacement of Short Single-Channel Electrode With Another Short Single-Channel Electrode. Although it was not the primary thrust of this survey, mention should be made of the consequences of replacing a short intracochlear electrode, such as the

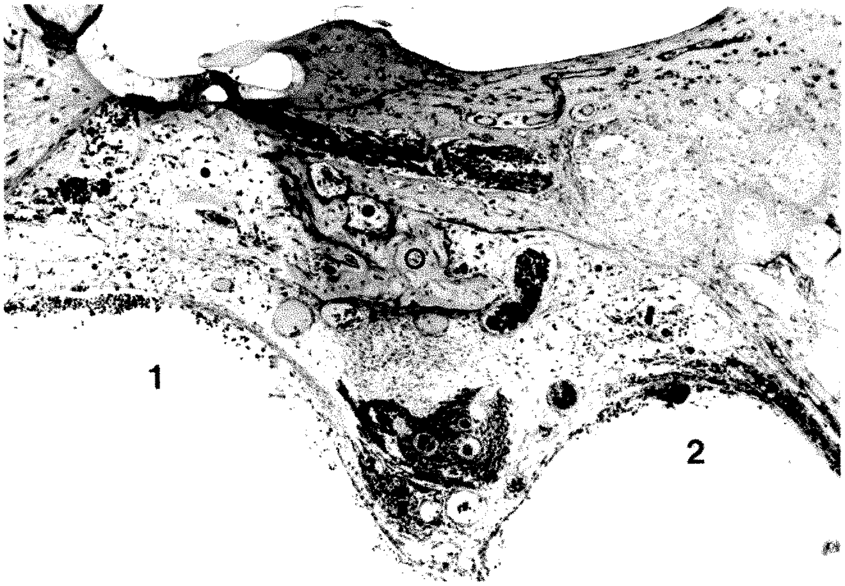

Fig 3. Radial section from basal turn of cat cochlea implanted with long electrode, which was removed after 2 months and replaced with identical device. 1 — initial electrode track, 2 — site occupied by second electrode, O — osteoneogenesis subjacent to osseous spiral lamina.

3M Alpha device (6 mm long), with another of the same design. As of the end of 1988, 294 children and approximately 750 adults had been implanted with 3M single-channel systems. Reimplantation has been performed with some frequency, in most instances because of device failure. Many failed 3M devices were revised with a wire-splicing technique that did not require replacement of the intracochlear electrode. In cases in which the intracochlear electrode was replaced, difficulty with reinsertion was reported in only one of approximately 25 cases related by survey responders. In this case, the original procedure had required drill excavation of an obliterated cochlear lumen to create a passage for the implant. Upon reimplantation, the osseous obliteration had recurred, and the indwelling wire resisted extraction, causing the distal ball electrode to be avulsed from its lead wire. Reinsertion was accomplished only after a repeat drill excavation of the basal turn. In the great majority of single-channel reimplantations the second insertion proceeded without difficulty, except for the occasional need to remove scar tissue or granulation tissue from the round window, a maneuver that did not affect functional results adversely.

The 3M Vienna device is also a single-channel system with a 6-mm electrode. One case in which such a device was replaced was uncovered in the survey, and this reimplantation was accomplished without difficulty.

Replacement of Short Single-Channel Electrode With Long Multichannel Electrode. Thirty-five cases were identified in which 3M devices, either

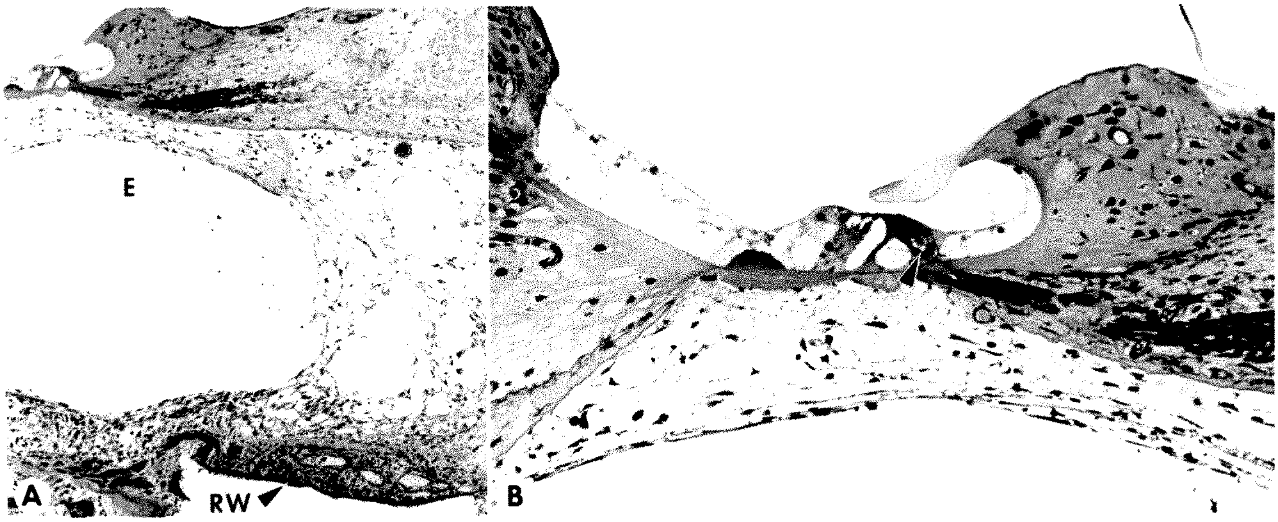

Fig 4. Long-to-long reimplantation case. A) Section through basal turn showing area occupied by implanted electrode (E). Lower portion of micrograph shows remnant of round window membrane (RW), which is thickened and edematous. However, scala tympani above it is relatively devoid of inflammatory cells, and spiral ganglion cells appear normal (upper right of micrograph). B) Fibrotic connective tissue capsule has formed over electrode, shown under intact organ of Corti. Cytoarchitecture of organ of Corti appears relatively normal, with recognizable hair cells, although inner spiral bundle region under inner hair cell is vacuolated (arrowhead).

the 6-mm Alpha or the older, 12-mm Sigma model, were replaced by Nucleus multichannel cochlear implants. Successful insertion of the longer device was accomplished in every case. Fenestration of the basal scala tympani was occasionally necessary to overcome scar or granulation tissue at the cochlear entry. The most extensive experience with replacement of single-channel implants with multichannel devices was reported by the House Ear Institute. Thirteen adults and ten children had single-channel 3M implants (17 Alpha, five Sigma, one model uncertain) replaced by Nucleus devices. The performance of these reimplanted systems, in terms of functional rehabilitation, appears to be comparable to that achieved with one-time multichannel implantation (J. A. Brimacombe, Cochlear Corp, unpublished data, November 1988).[1]

Three patients were identified who received a Symbion device after removal of a 3M implant. All three had uncomplicated reinsertions of the longer device and achieved satisfactory functional results.

Replacement of Long Multichannel Electrode With Another Long Multichannel Electrode. In our opinion, this category of reimplantation is the most critical for the future of cochlear implantation. Some experience with reimplantation was available for all four major multichannel devices. The most frequently implanted multichannel cochlear implant reported in this study was the Nucleus device (Cochlear Corp), which had been placed in 1,100 patients in North and South America by the end of 1988. Thirty-one patients have undergone reimplantation — an incidence of 2.8% for the series. The reasons for device replacement include device failure (12), skin flap complication (ten), misinsertion or compression of the electrode array (seven), trauma with hematoma at the receiver site (one), and accidental dislodgement during revision surgery to place a magnet on the standard receiver system (one). Information concerning the reimplantation procedure was available for 21 of the 31 cases. In 20 cases reinsertion was achieved uneventfully. In one reported case, reimplantation did not take place immediately after explantation. When insertion was attempted after a 1-month delay, some resistance was felt to the passage of the electrode. Nevertheless, full insertion was accomplished, and there was a good functional result.

The Symbion device (Richards Corp) had been implanted in 150 patients through the end of 1988, with five patients undergoing reimplantation (3.3%). Two implants were removed because of device problems, two because of traumatic shearing of the percutaneous pedestal, and one because of infection. Four of the five reimplantations were with second Symbion devices, and one with a Nucleus device. In two of the five reimplantations, the second insertion achieved normal cochlear penetration depth. In one case, slightly less than full insertion was achieved, with only five of six electrodes placed into the cochlea. In another case, explantation of the original implant was difficult, requiring a firm grip with a surgical clamp to effect extraction.[2] The lead wire trunk broke at 8 to 12 mm, leaving the apical portion along with three ball electrodes in the cochlea. The reimplanted electrode, which in this case was a Nucleus device, could be inserted only 75% of its usual length. Stimulation of the three apical electrodes of the Nucleus implant resulted in a facial motor response. Nevertheless, the patient gained considerable benefit using the middle portion of the array, which lay in the basal scala tympani. In the fifth case, major problems with reinsertion were encountered. In order to control a mastoid infection, the entire device had to be removed. Three months later, replacement was attempted, but misinsertion occurred. A second reimplantation attempt succeeded in placing only two electrodes in the cochlea, which was obliterated with fibrous tissue. The patient suffered a major decrement in auditory capabilities compared with performance levels prior to device replacement.

In the University of California, San Francisco (UCSF), series (Storz Corp), a total of 30 patients were implanted with two reimplantations (7%). Both of these were performed to replace failed devices. The first patient underwent reinsertion of another UCSF device without difficulty. A second patient, who had an early prototype system, underwent reimplantation with a Nucleus device during a two-stage procedure. In the first stage, the surgeon removed the antenna-receiver package and cut the electrode at the level of the round window. Subsequently, explantation and reimplantation were performed uneventfully.

One form of the Vienna device, although it is not a true multichannel system, possesses a long intracochlear electrode. Two patients who underwent successful reimplantation with this device have been reported previously.[3] One additional successful case was identified during this survey.

DISCUSSION

The removal of an indwelling cochlear implant electrode followed by reinsertion of a new device has been a maneuver of uncertain consequences to the cochlea and its surviving neural population. A scala tympani electrode may become encased in a fibrous envelope of variable density. Osteoneogenesis also is found frequently in the scala tympani, which may further stiffen the cuff surrounding the implant. From histologic studies of both human and animal cochleas, it is evident that this peri-implant fibrous sheath usually remains in situ following extraction of the electrode.[4-11] This fibro-osseous tissue theoretically may help reimplantation by channeling the replacement electrode atraumatically into the scala tympani. It may constitute a physical barrier that affords some protection to usually delicate intracochlear structures such as the basilar membrane and osseous spiral lamina. Additionally, by directing the new electrode to a location similar to the explanted one, it may help to re-create the previous electrode's orientation to neural structures. This may be important in patients who have learned to utilize optimally signals presented in a particular spatial orientation. Theoretically, the peri-implant sheath also may hinder replacement of an intracochlear electrode under certain circumstances. When the replacement electrode is either substantially longer or wider than the initial electrode, the surrounding tissues may render insertion of the new device difficult or impossible to achieve atraumatically.

The results of experimental implantation of cats were somewhat variable, but do suggest that replacing an implanted device may be achieved without adverse consequences to the cochlea, at least in some cases. However, a roughly twofold increase in traumatic insertions was seen in twice-implanted ears. Difficulty with reinsertion in these cases was probably the result of granulation tissue in the round window and basal scala tympani. Dissection of this tissue resulted in bleeding that rendered reimplantation more difficult. In one case, this pathologic reaction helped to channel the replacement electrode along a path different from that taken by the initial electrode. Gelfoam packing around the electrode in the middle ear, which was not used in every case, seemed to be related to the formation of round window granulation tissue. Unfortunately, there was no obvious way of determining a priori which patients would develop severe granulation tissue and present reimplantation difficulties. In the animal study, reimplantation also was associated with a greater degree of middle ear inflammation, although this is probably an artifact of the short period of time between the second implantation and histologic analysis.

The results of the clinical survey of reimplanted ears are considerably more reassuring than those of the animal study. Replacement of short single-channel electrodes with long multichannel ones was accomplished successfully in every case reviewed. One might expect that the peri-implant cuff in the basal scala tympani would present a barrier to reinsertion with a longer device. There are two apparent reasons why this was not a problem in the replacement of single-channel devices. The intracochlear portion of a single-channel implant is a thin, bare wire that resides in a short envelope that essentially constitutes a 6-mm-long diverticulum of the middle ear. Because it is so short and thin, the peri-implant sheath may be more likely to be extracted along with the device during removal. Also, most single-channel implants have a ball electrode at their tip that tends to grasp the surrounding fibrous cuff, further facilitating its extraction during electrode removal. Even when the peri-implant tissue remains in situ in the basal scala tympani following removal of a single-channel electrode, it is not an insurmountable obstacle for the implant surgeon attempting to place a long multichannel device. The surgeon can fenestrate the basal turn progressively until a lumen sufficient for insertion of the longer electrode is formed beyond the constriction created by the original device. This is a standard maneuver during the insertion of some multichannel devices.[12-15]

Sufficient clinical experience now has been accumulated to conclude that replacement of a long multichannel electrode with one of similar length and diameter is a relatively safe maneuver under most circumstances. Such a reinsertion ultimately may prove, with further experience, to be safer than primary implantation, as the peri-implant fibrous sheath may tend to minimize the chances of cochlear damage. However, revision cochlear implant procedures may pose additional surgical challenges due to formation of scar tissue within the facial recess, middle ear, and scala tympani. Care must be taken while reopening the facial recess to avoid injury to the facial nerve, particularly when the fallopian canal has been opened during the previous surgical exposure.

Clinical experience indicates that under certain circumstances, the peri-implant fibro-osseous cuff may hinder the atraumatic reinsertion of a cochlear implant electrode. Problems have been encountered in two situations. When explantation is not followed immediately by reimplantation, the peri-implant cuff tends to collapse and create a luminal restriction. This condition was reported in several clinical cases in the survey. When immediate reimplantation is not feasible, the surgeon should cut the electrode at the level of the round window, leaving the intracochlear portion in place to serve as a lumen-keeper. The second circumstance in which reimplantation may be a problem is when the indwelling electrode does not have a smooth external surface. Electrode contact surfaces that protrude from the Silastic-coated wire bundle may become encased in fibrotic tissue and impede electrode removal. They even may shear off and remain behind in the scala following electrode extraction. In anticipation of future explantation and reimplantation, all intracochlear electrodes should have contact surfaces that are flush with the electrode carrier and firmly anchored in place.

Future multichannel devices are likely to utilize electrodes that are longer, and possibly wider, than contemporary multichannel implant systems. Theoretically, when reinsertion is attempted with an electrode that is substantially longer and/or wider than the previous one, atraumatic replacement may not be possible. Significant data do not yet exist for this type of cochlear reimplantation, as most removed multichannel electrodes have been replaced with electrodes of length and diameter similar to those of the original one. Forceful attempts to insert an electrode beyond an established peri-implant sheath may damage delicate electrode contact surfaces, cause injury to the cochlea that further depletes neural elements, or result in the electrode's folding back on itself and becoming malpositioned. Ideally, all devices should be designed to penetrate the cochlea to a depth exceeding 25 mm in order to permit stimulation across the entire frequency range of human speech. Further, with maintenance of a maximal scalar lumen, the cochlea will remain receptive to future advances in multichannel electrode technology.

CONCLUSIONS

1. The results of animal studies indicate that cochlear explantation followed by immediate reimplantation may be accomplished without damage to the cochlea or its neural population, at least in some cases. Proliferation of granulation tissue in the round window and scala tympani, however, may cause difficulty in insertion of the replacement device and increase the likelihood of induced trauma.

2. In a significant clinical experience, reimplantation was accomplished without adverse consequences in the vast majority of cases. This includes replacement of short single-channel electrodes with long multichannel ones as well as replacement of indwelling long electrodes with new devices of similar length and diameter.

3. When a suitable replacement electrode is not available at the time of device removal, the electrode should be cut at the round window so as to leave the intracochlear portion in place to maintain the scala tympani lumen. Explantation followed by delayed reimplantation may be complicated by compromised cochlear patency.

4. Future devices should be designed to facilitate their eventual explantation and replacement. Electrode carriers should possess a smooth surface without protruding electrodes that may be dislodged during extraction.

5. Contemporary multichannel electrodes should be of sufficient length and diameter to maintain a maximal scalar lumen for future use. The fibro-osseous sheath that forms around a long electrode may make its later replacement with an upgraded multichannel array that is either substantially longer or wider than the indwelling one difficult to achieve atraumatically.

ACKNOWLEDGMENTS — The authors thank the following individuals and their organizations for providing information used in the clinical survey: Judith Brimacombe (Nucleus Corp), Corine Dancowsky (Symbion Corp), Ralph Fravel (3M Corp), Karen Berliner and William Luxford (House Ear Institute), and Dorcus Kessler (University of California, San Francisco). We are also grateful to the numerous implant surgeons who shared their reimplantation experiences, to Henry Milczuk, who assisted with our review of the histologic materials, and to Gary Hradek for excellent technical assistance.

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NEW MICROLARYNGEAL INSTRUMENTS FOR PHONATORY SURGERY AND PEDIATRIC APPLICATIONS

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A new microlaryngeal instrument set has been developed for phonatory surgery in adults and for pediatric laryngology. This 20-instrument set consists of forceps (cupped and alligator type) and scissors with 1-mm distal grasping and cutting tips. Open tip and whistle tip variety suction instruments with tip diameters of 1.0, 1.5, and 2 mm are also available. Included as well are fine (1.0-mm) probes for palpation and laser welding and smoke evacuation double-action grasping forceps. This microlaryngeal instrument set has been extremely useful in more than 80 clinical applications.

KEY WORDS — microlaryngeal instruments, phonatory surgery.

Few changes in microlaryngeal instrumentation have occurred since the introduction and subsequent popularity of the surgical laser (carbon dioxide) in the mid-1970s.[1] Various designs of operating laryngoscopes have been introduced over the past 10 years — many for special exposure of the adult and pediatric anterior and posterior commissures and subglottic larynx.[2] Advances also have taken place in the refinement of the laser spot impact size. A new CO2 laser micromanipulator is now available that delivers a laser beam as small as 300 μm (0.3 mm) using a 400-mm lens on the operating microscope.[3] When this smaller spot size laser delivery system is used, microflap techniques for the treatment of patients with laryngotracheal stenosis, Reinke's space edema, and polypoid vocal cord changes are possible.[4] Reducing the laser spot diameter also has improved the results of pediatric microlaryngeal surgery. Unfortunately, standard microlaryngeal instruments with 3-mm grasping forceps jaws, scissors, and suction tips are not suitable for these fine techniques. With these indications and needs in mind, a 20-instrument set of microlaryngeal instruments has been designed and developed with Karl Storz Endoscopy-America, Inc, Culver City, Calif.

INSTRUMENTATION

This microlaryngeal instrument set has been designed for atraumatic microlaryngeal surgery with or without a surgical laser. The instruments feature reinforced proximal shafts with a working length of 20 cm. Distal grasping tips are 1 mm in length and include cupped and alligator-type jaws in straight, angular (up-grasping), and right- and left-angled designs (Fig 1). Fine (1-mm) scissors complement the currently available standard 3-mm variety (Fig 2).

Open tip microlaryngeal suction instruments are

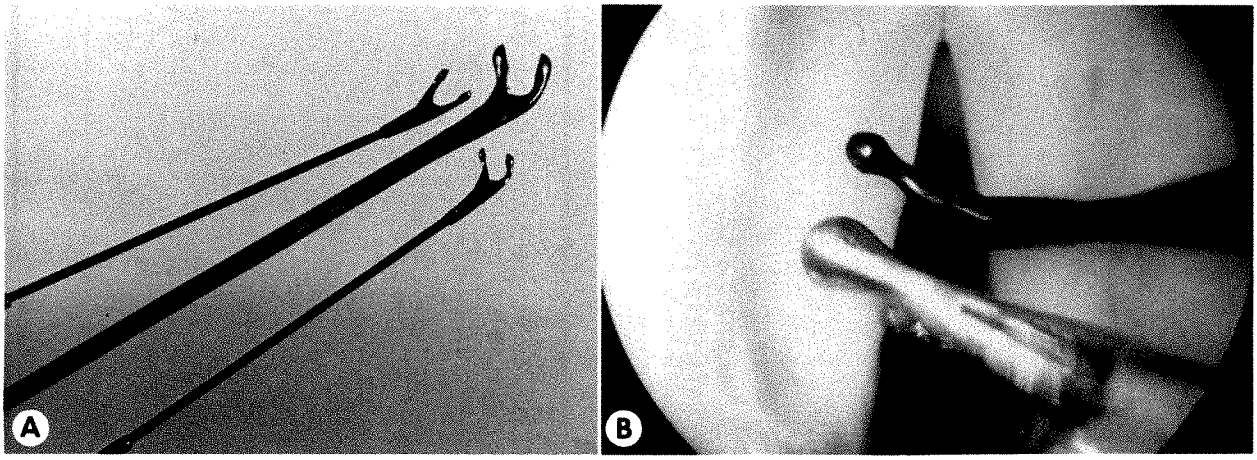

Fig 1. New microlaryngeal forceps with 1-mm grasping jaws. A) In comparison with standard forceps (middle). B) With standard forceps (bottom), grasping free edge of larynx from calf cadaver.

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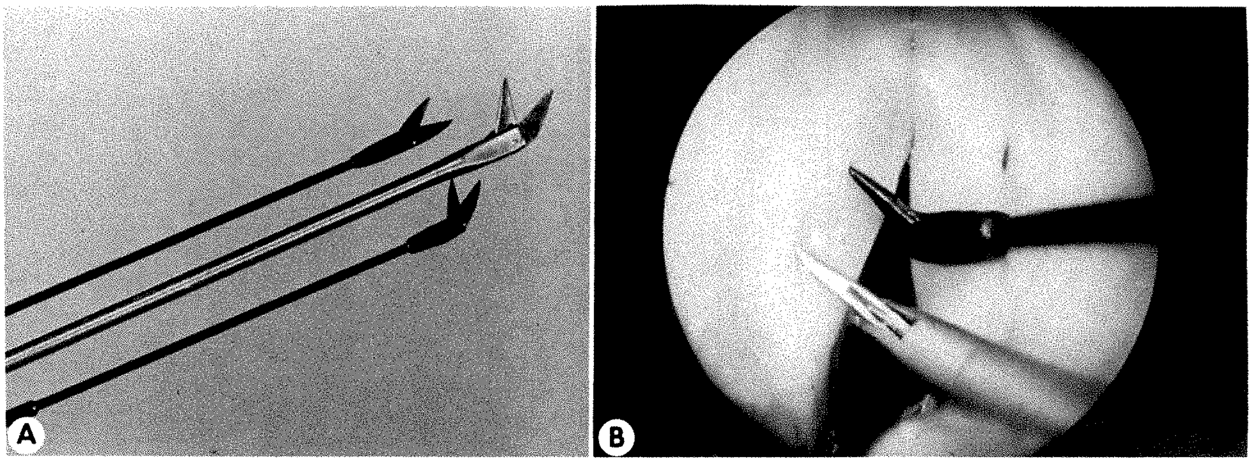

Fig 2. Microlaryngeal scissors. A) Straight and upturned shown in comparison with standard upturned scissors (middle). B) Delicate upturned, 1-mm (top), seen next to standard scissors. Both are poised to cut left vocal cord.

available with tip diameters of 1.0, 1.5, and 2.0 mm for atraumatic removal of secretions as well as evacuation of myxoid secretions from polypoid vocal cords. Whistle tip variety suction instruments are also available with the same diameters (Fig 3). These are useful as atraumatic blunt tissue probes and for smoke evacuation during laser surgery. The microsuction instruments have triangular openings on the proximal shaft that permit the thumb to vary the amount of suction applied. This fine control limits the traumatic effect of excessive suction on the mucosal membranes and underlying vocalis muscle.

Microlaryngeal probes are 1.0 mm in tip diameter and are available in straight and 45°-angled distal ends. These delicate probes give the endoscopist a more precise sense of palpation for an accurate detection of induration, tissue mass, and cystic changes. The probes are also useful for breaking up thick myxoid fluid in Reinke's space before suctioning (Hirano technique).[4]

Two special forceps have been developed for precise microlaryngeal laser surgery: one for the welding of mucosal edges, and the other for fine grasping and simultaneous built-in smoke evacuation. The welding forceps are designed with a horizontal 1-mm grasping tip with a 0.5-mm space between the jaws. A small spot (300 to 500 μm) CO_2 laser with milliwatt capability can be used to weld epithelial edges coapted with the forceps. The laser smoke evacuator on the forceps removes any hot smoke at the time of laser impact, preventing adjacent tissue heat coagulation in addition to freeing the endoscopist's opposite hand for adjusting the micromanipulator control.

DISCUSSION

This microlaryngeal instrument set has been extremely useful in more than 30 adult and 50 pediatric applications. Greater precision has been achieved in the treatment of vocal cord nodules, polyps, polypoid changes, respiratory papillomatosis, excision of hyperkeratosis, diffuse dysplasia, and glottic-subglottic stenosis.

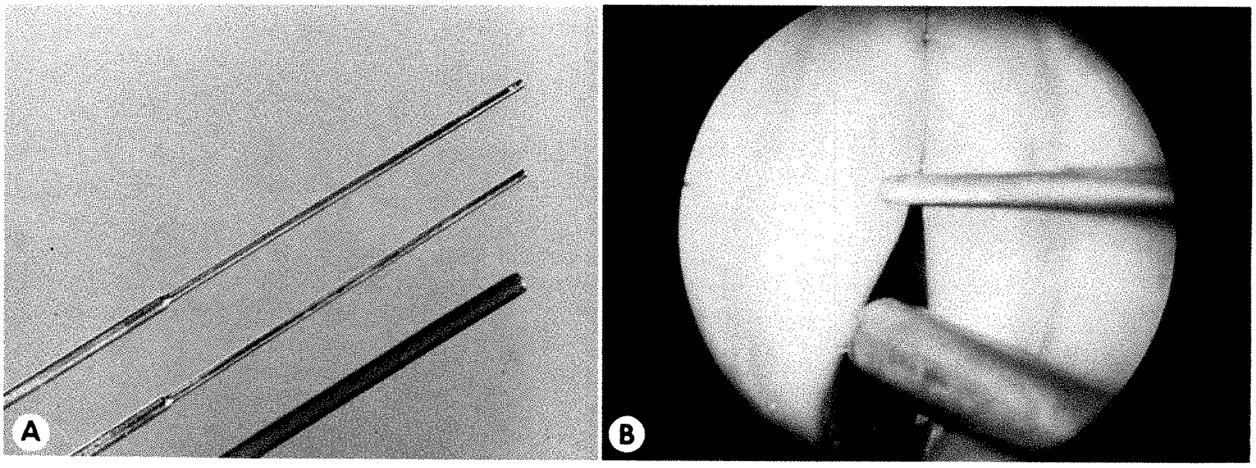

Fig 3. Microlaryngeal suction instruments. A) New whistle tip and open tip 1.0-mm instruments shown next to more standard 3-mm suction instrument. B) Open tip suction instruments seen in A shown applied to left vocal cord. Triangular openings on proximal end of new suction instruments permit thumb to control degree of suction.

These instruments facilitate the creation of a mucosal microflap for preservation of the mucous membrane covering. A typical operating room instrument setup for adult patients includes the new microinstruments as well as larger standard instruments. The standard instruments are more useful for larger lesions, such as carcinomas and granulomas, as well as florid exophytic papillomatosis. Larger grasping forceps are necessary for adequate deep biopsy and broad grasping of tissue. The new, more precise instrument set is more useful for phonatory surgery and pediatric laryngology.

Just as smaller osteotomes have refined rhinoplastic surgery, we hope these new microlaryngeal instruments will improve operative results in laryngology. Similar in size to otologic forceps and suction probes at their working end, these instruments have become our standard tools for laryngeal phonatory surgery and pediatric applications.

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INTERNATIONAL CONFERENCE AND WORKSHOP HEAD AND NECK CANCER REHABILITATION

An International Conference and Workshop on Head and Neck Cancer Rehabilitation will be held March 14-18, 1990, at the Ritz Carlton Hotel in Dearborn, Michigan. For further information, contact Department of Otolaryngology, Wayne State University, School of Medicine, 4201 St Antoine, 5E - UHC, Detroit, MI 48201; (313) 577-0804.

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DELAYED AIRWAY OBSTRUCTION AND NECK ABSCESS FOLLOWING MANUAL STRANGULATION INJURY

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Few reports describing manual strangulation injury to the neck are found in the otolaryngologic literature. Since most victims sustain immediate fatal asphyxiation, brain anoxia, or cardiac arrest, they are usually examined by a forensic pathologist. When strangulation attempts are nonfatal, neck injuries can lead to delayed airway obstruction. If not managed in a timely fashion, these injuries can be fatal or cause permanent laryngotracheal sequelae. We describe a patient who 36 hours following manual strangulation developed acute upper airway obstruction and neck abscess necessitating tracheotomy, neck exploration, and drainage. Patients suffering this unique type of compression injury may present initially with deceptively benign symptoms and signs. We discuss the overall management of these patients, stressing the need for early imaging studies, endoscopic assessment, and continued airway monitoring in an intensive care unit.

KEY WORDS — blunt neck trauma, laryngotracheal trauma, neck abscess, neck injury, strangulation.

INTRODUCTION

It has been estimated that between 5% and 10% of criminally violent deaths in large urban areas are due to strangulation.[1] In 1987 alone, 293 documented deaths were caused by strangulations, hangings, and suffocations in New York City. Of these, 23% were due to strangulation and hanging homicides.[2] While the overall incidence of blunt neck trauma due to motor vehicle accidents is declining, the number of personal assaults, often associated with inner-city, drug-related (cocaine) violence, is increasing. Therefore, strangulation, rather than accidental trauma, will likely be responsible for an increasing proportion of these injuries.[3]

Manual strangulation is a form of blunt neck trauma that is encountered infrequently by the otolaryngologist–head and neck surgeon. This type of injury is more often a postmortem curiosity for the forensic pathologist, since the majority of victims sustain asphyxiation, cardiac arrest, or fatal brain anoxia. When strangulation attempts are nonfatal, neck injuries lead to a spectrum of upper aerodigestive tract sequelae unique to the duration and type of compressive forces generated. A patient with a history of strangulation may appear asymptomatic and deceptively without external neck or mucosal injuries. Therefore, the extent of soft tissue, neurovascular, and cartilaginous injury frequently is underestimated during emergency room evaluation, especially if airway distress is absent. When unrecognized, these injuries can lead to delayed fatal airway obstruction that may occur more than 24 hours following the initial injury.

The overall management of these patients is discussed, with emphasis on the need for early imaging studies, endoscopic assessment, and continued airway monitoring in an intensive care unit.

CASE REPORT

During an assault, a 45-year-old man was placed in a "choke hold" and strangled for 30 seconds. After an asymptomatic period of 36 hours, he presented to the emergency room in mild respiratory distress with slight stridor on deep inspiration and a muffled, hyponasal voice. His vital signs on admission were normal. There was extensive cervical and facial edema extending from the periorbital region to the supraclavicular fossa (Fig 1). His neck was diffusely tender, nonfluctuant, and without subcutaneous emphysema. Considerable trismus made intraoral examination difficult. The soft palate and oropharynx were diffusely edematous, and the uvula was twice its normal size. The palate was nonfluctuant and there were no exudates or dental caries. Saliva from Stensen's and Wharton's ducts was clear. The admission WBC count was 10,000/mm^3 with a shift to the left. Lateral neck and facial radiographs demonstrated diffuse soft tissue swelling. There were no fractures or dislocations of the cervical spine or mandible. Tracheal deviation was seen on chest radiography. Because of progressive airway distress, the patient was transferred to the operating suite, where a tracheotomy was performed under local anesthesia. Massive oropharyngeal and supraglottic edema would not allow direct laryngoscopy or esophagoscopy.

A neck exploration revealed diffuse inflammation and edema involving all fascial planes. The carotid sheath and parapharyngeal space were explored and failed to reveal an abscess. However, dissection of the right submandibular space yielded several milliliters of purulent fluid. Cultures were performed for acid-fast bacilli, fungi, actinomycosis,

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Presented at the meeting of the American Broncho-Esophagological Association, San Francisco, April 3-4, 1989.

REPRINTS — Daniel B. Kuriloff, MD, Dept of Otolaryngology, Division of Head and Neck Surgery, University of Michigan, Ann Arbor, MI 48109.

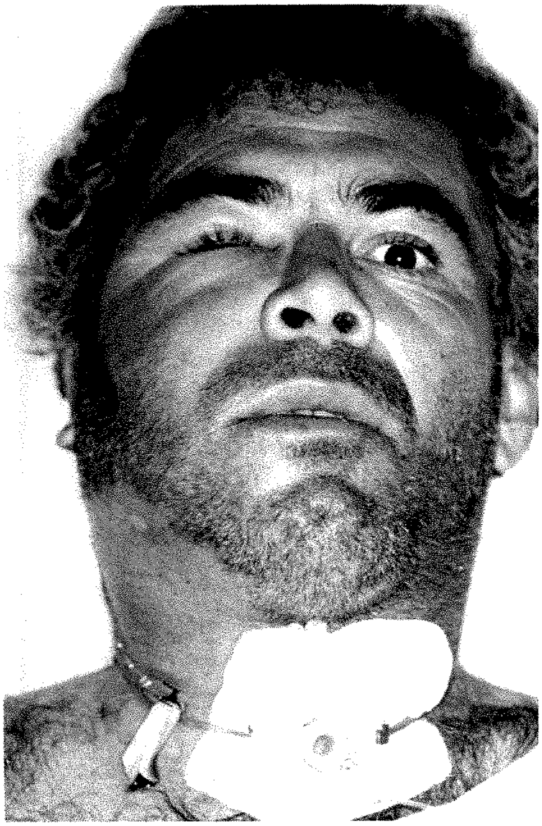

Fig 1. Manual strangulation victim with right-sided cervicofacial edema (immediate postoperative appearance).

and aerobic and anaerobic bacteria. Multiple Penrose drains were placed, and intravenous cephalothin sodium was started. Intraoperative cultures subsequently identified group A *Streptococcus*. Computed tomography of the neck revealed substantial compression and deviation of the oropharynx and upper airway accompanied by diffuse soft tissue edema (Fig 2). There were no residual fluid collections or fractures of the hyoid bone, thyroid cartilage, or cricoid cartilage. Oral intake was suspended over the next several days. The patient's neck edema resolved, and he was decannulated uneventfully on the fifth hospital day. His diet was advanced slowly from clear liquids and was well tolerated. Two weeks following discharge the tracheotomy site was healing well and his voice was normal. Indirect laryngoscopy revealed normal vocal cord position and mobility.

DISCUSSION

Mechanics of Injury. Hanging should be distinguished from strangulation, in which the victim is not suspended and body weight plays no role. Strangulation may be effected by three methods: 1) the use of bare hands, also known as manual strangulation or throttling, 2) the elbow bend compression, choke hold, or stranglehold, and 3) the use of a ligature or iron collar (garotting). Strangulation injury is produced by either concentric pressure

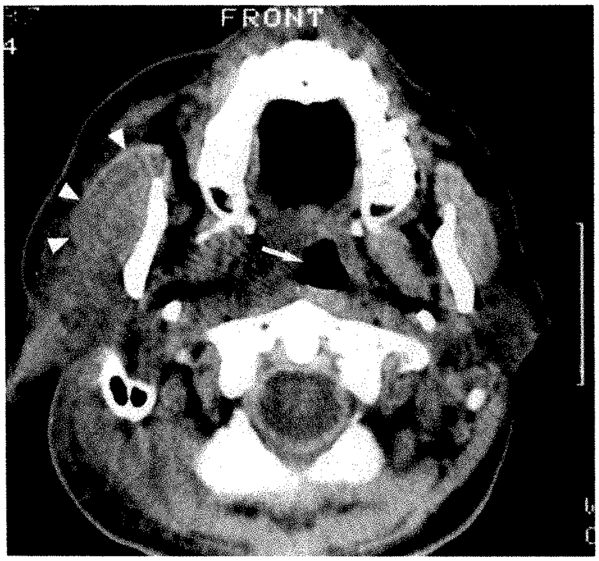

Fig 2. Axial computed tomogram of neck at level of oropharynx. Diffuse soft tissue edema has compressed oropharyngeal airway (arrow) and expanded masseter muscle on right (arrowheads).

applied to the neck or anterior compression against the vertebral column. The compressive forces generated during a manual strangulation attempt are highly variable. The exact cause of death for any one victim is often unknown, but may be due to asphyxiation, vascular insufficiency causing brain anoxia, or a vagally mediated cardiac arrest. Any of these factors in combination may be incriminated.

The specific injury to neurovascular, cartilaginous, and soft tissue structures depends upon the method of compression, the amount of force applied, and the duration of application.[4] A gamut of these injuries is described in the forensic pathology literature.[5,6] External signs of strangulation range from no visible changes to extensive skin injury such as abrasions, contusions, and fingernail scratches. Signs of vascular congestion may include skin, mucosal, and subconjunctival hemorrhages. These may manifest as petechiae, ecchymoses, or hematomas. Engorgement and edema of the oropharynx, tongue, and supraglottis above the area of constriction often are seen and may cause airway compromise.[6] Peppard[7] described four patients with vocal cord paralysis following strangulation injury. Vocal cord paralysis was usually transient, with full recovery occurring within 4 to 20 days. The lesion is believed to represent a compression-induced neuropraxic neuropathy of the recurrent laryngeal nerve. Muscular and fascial soft tissue contusion commonly is seen, even when there are no external signs of injury, and may be localized or diffuse. Injury to the sternocleidomastoid and strap muscles is common and may lead to considerable edema.[4]

The hyoid bone and laryngeal cartilages are vulnerable to injury because of their anterior location in the neck. In addition to the compressive forces involved, the degree of ossification of the thyroid and cricoid cartilages will determine the likelihood of fracture. Calcification rarely begins prior to the third decade, and occurs earlier in men than in women.[8] Therefore, fractures of the laryngeal cartilages are unusual prior to the age of 20 and rare in children. Line et al[9] reviewed 112 strangulation deaths seen by the Los Angeles County Coroner's Office. Manual strangulation, rather than ligature strangulation, caused more fractures of the hyoid bone and laryngeal cartilages. The hyoid bone was fractured most frequently, followed by the thyroid cartilage. Most of the fractures were nondisplaced, involved the superior cornua of the hyoid bone or the thyroid lamina, and occurred twice as often in women as in men. In their series, nine patients had fractures of both the hyoid bone and thyroid cartilage, while only one patient had fractures of both of these and the cricoid. Severely displaced fractures of the thyroid and cricoid cartilages usually are associated with mucosal lacerations and hematomas, and may lead to airway collapse and immediate asphyxiation.

Carotid intimal injuries rarely occur and are seen more often with hanging. Carotid artery thrombosis and atheromatous embolization rarely may cause cerebrovascular accidents.[5,6] Global brain ischemia and hypoxia in survivors usually leads to coma and rapid death. Neuropathologic examination demonstrates severe encephalomalacia, multiple cystic infarcts, parenchymal and subarachnoid hemorrhages, and generalized ventricular dilatation.[10] A pressure-mediated vagal response, possibly mediated through the carotid sinus, may cause collapse and cardiac arrest resistant to resuscitative efforts. Postobstructive pulmonary edema and cervical spine injuries seldom are seen with manual strangulation, but are not uncommon following hanging.[6]

Clinical Presentation. Because of the slowly compressive nature of the forces involved in strangulation, victims may present with deceptively innocuous signs and symptoms. There may be no or minimal external manifestation of soft tissue trauma. The upper airway also may appear normal beneath intact mucosa, despite hyoid bone or laryngeal fractures. The patient presented in this report developed delayed upper airway obstruction due to massive engorgement and edema of the supraglottic and oropharyngeal soft tissues 36 hours following his initial injury. Despite the absence of hyoid bone or laryngeal fractures, soft tissue trauma alone led to upper airway compromise. The source of the submandibular space abscess is unclear, but it may have developed from submandibular gland injury.

Delayed edema, hematoma, vocal cord immobility, and displaced laryngeal fractures all may contribute to an unstable airway following strangulation. Stanley and Hanson[11] described a strangulation victim who was seen 36 hours after the injury and had no external signs of trauma. Indirect laryngoscopy revealed bilateral vocal cord paralysis and mucosal edema without lacerations. A CT scan of the neck demonstrated vertical fractures of both the thyroid and cricoid cartilages. Despite return of vocal cord motion, the patient remained aphonic because of lateral displacement of the cricoarytenoid joint. Another strangulation victim in their series developed delayed edema and airway obstruction due to an infected laryngocele. Slowly progressive supraglottic, pharyngeal, and tongue edema also can contribute to variable degrees of delayed airway obstruction.

SUMMARY

Strangulation represents a unique type of blunt neck trauma involving slowly compressive forces. Posttraumatic symptoms and signs may be insidious. Head and neck examination must be complete, and include neurologic assessment for every patient. Although cervical spine injury is unusual in this setting, the neck should be immobilized until fractures and dislocations are evaluated by radiography. Airway evaluation should be a priority in these patients. Signs and symptoms of laryngeal fractures must be assessed and include subcutaneous emphysema, hoarseness, hemoptysis, otalgia, dysphagia, point tenderness and swelling over the larynx or hyoid bone, crepitation, and palpable fractures. Initial anteroposterior and lateral radiographs of the neck are useful; however, CT is the preferred imaging study for laryngotracheal trauma. On indirect or flexible fiberoptic laryngoscopy, mucosal tears, hematomas, exposed cartilage, and arytenoid and vocal cord displacement may suggest a fracture, and require further endoscopic, radiographic, or surgical evaluation. The method of immediate airway management in laryngotracheal trauma remains controversial, with proponents for both tracheotomy and translaryngeal intubation.[3] In general, an orderly tracheotomy is our preferred approach. All patients with a history of strangulation, without dyspnea on presentation, should be monitored in an intensive care setting for at least 24 hours. Periodic flexible fiberoptic laryngoscopy should be performed routinely for continued airway monitoring.

It is essential that emergency room personnel and consulting otolaryngologists be familiar with the nature and management of strangulation injury. A high index of suspicion for laryngotracheal injury and the potential for delayed airway obstruction in these patients is crucial. Early diagnosis, expedient airway management, and primary repair of laryngotracheal injuries will help prevent permanent or fatal laryngotracheal sequelae.

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THE FIRST INTERNATIONAL LARYNGOTRACHEAL RECONSTRUCTION SYMPOSIUM

The Cleveland Clinic Foundation is sponsoring a continuing education program entitled The First International Laryngotracheal Reconstruction Symposium, to be held August 24-27, 1991, at Stouffer Tower City Plaza Hotel in Cleveland. For further information, please contact The Cleveland Clinic Educational Foundation, Department of Continuing Education, 9500 Euclid Avenue, TT31, Cleveland, OH 44195-5241; 444-5696 (local), (800) 762-8172 (Ohio), (800) 762-8173 (outside Ohio).

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POSTTRACHEOTOMY GRANULATION TISSUE MANAGED BY CARBON DIOXIDE LASER EXCISION

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The problem of accumulation of granulation tissue and scar at the superior edge of the tracheostoma is a frequent problem in the management of chronic tracheotomy patients. This traditionally has been managed by cup forceps excision or by eversion through the tracheostoma with a skin hook and blind resection. These methods often lead to hemorrhage, and incomplete removal in a bloody field. We have used the carbon dioxide laser via a bronchoscope for ablation of the granulation tissue and/or scar at the stomal edge and at the tracheotomy tube proximal tip without morbidity in 13 pediatric cases. With experience, removal with the laser often proceeds more quickly than conventional methods. The scar and granulation tissue are excised under direct vision with minimal hemorrhage. We believe this to be a reasonable alternative in the management of this recurring problem.

KEY WORDS — granulation tissue, laser, tracheotomy.

INTRODUCTION

The management of posttracheotomy granulation tissue is a problem encountered frequently by otolaryngologists. In the pediatric population its reported incidence as a late complication of tracheotomy is between 1/294 and 50/319 (15.7%).[1,2] One report suggests that it is so common that it may be considered a routine finding and not a complication at all.[3] This granulation tissue may be a source of bleeding, may cause difficulty in replacing the tracheotomy tube, may delay decannulation, and may cause obstruction. Granulation tissue obstructing the tracheotomy tube has been cited as a cause of death in several patients.[4]

Several methods are used to remove this granulation tissue from the lumen of the trachea. The most direct is cup forceps removal via the bronchoscope. This technique is accompanied by attendant bleeding and is often difficult for residents to master. The technique previously employed at Children's Hospital of Pittsburgh used a skin hook to grab the suprastomal granulation tissue and evert it through the tracheostoma, then excise it with scissors. This technique also had problems with bleeding and with exposure of the granulation tissue, and required another trained assistant to perform. This technique has been facilitated by the use of the endoscopic camera so that the surgeon may visualize the granulation tissue prior to securing it with the skin hook.

In consideration of these difficulties with bleeding and exposure of the granulation tissue, we began to use the carbon dioxide laser through the ventilating bronchoscope to ablate tracheal granulation tissue. We present the results of our initial series in the pediatric age group using this alternative technique.

MATERIALS AND TECHNIQUE

A Sharplan 1100 CO_2 laser attached to a Wolf bronchoscope via a laser coupler was used in the 13 cases (12 patients). The only entry criterion was the ability to use the smallest 4.0 Wolf bronchoscope to give exposure to the site of granulation tissue.

The patient's plastic tracheotomy tube was replaced with a metal tracheotomy tube, and the patient was draped with wet towels. The tissue was ablated with laser powers of 15 W in pulses of 0.05 seconds, or at 10 to 15 W continuous power. The beam was used in the focused mode for ablation, and was defocused slightly for any areas requiring more hemostasis.

The additional time for the preparation of the laser added less than 10 to 15 minutes to the procedure. There were no major modifications to standard laser bronchoscopy technique, but we found that preheating the spit window with very hot water prevented fogging of the lens.

RESULTS

A total of 13 operations were performed on 12 patients. There were eight boys and four girls. The ages ranged from 7 months to 17 years, and the duration of tracheotomy tube placement ranged from 6 weeks to 3 years (see Table). Only one patient did not have a tracheotomy tube in place. This patient was status post anterior laryngotracheal decompression and was the only patient requiring two procedures. Visualization was excellent in all pro-

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Presented at the meeting of the American Broncho-Esophagological Association, San Francisco, April 3-4, 1989.

REPRINTS — Sylvan E. Stool, MD, Dept of Pediatric Otolaryngology, Children's Hospital of Pittsburgh, 3705 Fifth Ave at DeSoto St, Pittsburgh, PA 15213.

SUMMARY OF CASES

Patient	*Age*	*Weight (kg)*	*Diagnosis*	*Tracheotomy Tube*	*Duration of Tracheotomy*	*Site of Granulation Tissue*
1*	7 mo	7.3	Subglottic stenosis†	—	9 d	Cricoid
2	18 mo	9	Orthotopic liver transplant, respiratory insufficiency	No. 1 Shiley pediatric	6 wk	Stomal
3	2 yr	9	Subglottic stenosis	No. 1 Shiley pediatric	3 mo	Stomal
4	3 yr	15	Bronchopulmonary dysplasia	No. 4 Shiley pediatric	2 yr	Stomal
5	3 yr	16	Subglottic stenosis	No. 2 Shiley pediatric	5 mo	Stomal
6	4 yr	17	Papilloma	No. 3 Shiley pediatric	12 mo	Stomal
7	4 yr	16	Papilloma	No. 3 Shiley pediatric	2 yr	Stomal
8	5 yr	16	Encephalitis, respiratory insufficiency	No. 2 Shiley pediatric	2 mo	Stomal
9	4 yr	26	Acquired subglottic stenosis	No. 3 Shiley pediatric	15 mo	Tracheal
10	12 yr	55	Post–motor vehicle accident, respiratory insufficiency	No. 6 Shiley cuffed	4 mo	Stomal, tracheal
11	14 yr	44	Cerebral palsy	No. 4 Shiley pediatric	12 mo	Stomal
12	17 yr	29	Muscular dystrophy	No. 7 Harlake	4 yr	Stomal

Follow-up ranged from 3 to 18 months.

*Only patient requiring two procedures.

†Anterior laryngotracheal decompression performed. Granulation tissue was removed without tracheotomy tube in place.

cedures, and estimated blood loss was less than 2 mL in each case. Postoperative suctioning through the tracheotomy tube demonstrated a minimal amount of blood aspirated into the tracheobronchial tree, compared to that with conventional excision techniques. Six of the procedures were performed adequately by resident staff under attending supervision.

There were no cases of postoperative delayed hemorrhage or any other complications such as aspiration pneumonia or stomal stenosis. All patients were treated as outpatients. Repeat endoscopic procedures often are performed earlier than scheduled when patients have concerns about tracheotomy site bleeding, obstruction to suctioning, or difficulty replacing the tracheotomy tube. These repeat procedures appear to be necessary at longer intervals with this laser procedure.

DISCUSSION

The suprastomal edge of the tracheotomy site and the area at the tip of the tracheotomy tube are the most frequent sites for the formation of granulation tissue posttracheotomy.[2] The traditional explanation for this is local trauma due to tube motion or suction catheters and localized perichondritis. Several large studies of pediatric tracheotomies have reported various incidences. Oliver et al[1] in 1962 reported one case in 294 tracheotomies, and Hawkins and Williams[5] reported one case in 73. Tucker and Silberman[4] reported 18 cases in a review of 350 pediatric tracheotomies and noted that tracheal granuloma accounted for two deaths. Carter and Benjamin[3] in 1983 reported granulation tissue as a complication in 17 of 164 cases (10.4%) and commented that this occurred commonly enough to be considered a routine finding rather than a complication. In a 10-year review of 319 children, Crysdale et al[2] reported 29 cases of tracheal granuloma and 21 cases of stomal granuloma occurring as late complications of tracheotomy.

The granuloma at the stomal edge may cause bleeding, may obstruct tracheotomy tube changes, or may delay decannulation. The granuloma at the tip of the tracheotomy tube also may cause bleeding, airway compromise, or complete obstruction. Cup forceps removal of this granulation tissue usually is accompanied by moderate bleeding and often imprecise or incomplete removal. The excess blood may be aspirated distally and be a cause of postoperative atelectasis. Another technique of removal requires the use of an assistant to grab the stomal granulation tissue and evert it through the stoma for excision. This technique also has moderate to troublesome hemorrhage, and poor visibility through the stoma frequently occurs. Tracheal granulation tissue cannot be treated by this method.

The first report of bronchoscopic CO2 laser use by Strong et al[6] in 1974 included a report of the ablation of tracheal granulation tissue. The multi-institutional trial of the bronchoscopic CO2 laser coupler directed by Ossoff et al[7] included the treatment of nine patients with granulation tissue without complications. The advantages in the use of the CO2 laser include the ability to perform "hands-off" endoscopic surgery through a ventilating bronchoscope, precise control of the ablation, moderate hemostasis, and decreased perioperative edema.[8] In our institution, use of the laser has not added significantly to the procedure time, and is often faster than the eversion technique. Finally, it is a technique that can be taught and demonstrated easily to the house staff.

Disadvantages of this laser technique include the cost of the laser, experience of the operator, and the theoretic hazard of the laser plume. The major disadvantage to this laser technique is that there is a minimum size limit for the airway. The patient's airway must allow passage of a size 4.0 Wolf bronchoscope (outside diameter, 7.0 mm) or exposure of the suprastomal edge with a subglottiscope. This size limitation might be obviated with the use of the neodymium:yttrium aluminum garnet laser through a flexible fiber. Dumon et al[9] found this technique especially useful in the treatment of granulation tissue after sleeve resection of the trachea in five cases, and in ten cases of isolated granuloma.

CONCLUSION

The technique of bronchoscopic CO2 laser excision of tracheal and suprastomal granulation tissue has distinct advantages compared to conventional excision. Under direct vision, a precise ablation of the tissue may be performed with minimal hemorrhage. The lack of postoperative bleeding limits aspiration of blood. Finally, in contrast to the technique using the skin hook, it can be performed by the surgeon without an assistant. In selected patients (those with airways large enough) it is now our preferred method of treatment.

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SOFT TISSUE SURGERY WORKSHOP

The Cleveland Clinic Foundation is sponsoring a continuing education program entitled Soft Tissue Surgery Workshop, to be held February 1-2, 1990, at The Clinic Center Hotel in Cleveland. For further information, contact The Cleveland Clinic Education Foundation, Department of Continuing Education, 9500 Euclid Avenue, TT31, Cleveland, OH 44195-5241; 444-5696 (local), (800) 762-8172 (Ohio), (800) 762-8173 (outside Ohio).

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IMAGING CASE STUDY OF THE MONTH

MULTIPLE FRONTOETHMOID MUCOCELES

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CHICAGO, ILLINOIS

Mucoceles of the paranasal sinuses are composed of mucoid secretions and desquamated epithelium within a sinus, with distension of its walls. In most cases the cause of this condition is multifactorial. The most common mechanism involves obstruction of a sinus ostium due to chronic infection with or without polyposis, trauma, previous surgery, allergy, or tumor.[1] Persistent mucus production from the sinus mucosa results in expansion of the sinus and compression of adjacent structures. The most common location of mucoceles is the frontal and ethmoid sinuses.[1,2] Plain sinus radiography, computed tomography, and magnetic resonance imaging can aid in the diagnosis of frontoethmoid mucoceles.

We report a patient with multiple frontoethmoid mucoceles with intracranial extension. The bone imaging provided by CT was critical in the appropriate management of this complex mucocele.

CASE REPORTS

A 37-year-old man presented with a 7-month history of right eye pain and frontal headaches of increasing severity. He had a history of allergies and nasal polyps. He complained of complete anosmia, but denied any change in his visual acuity.

Physical examination revealed mild proptosis of his right eye, but his extraocular eye movements were intact. He had normal visual acuity and normal results on fundoscopic examination. Nasal examination revealed bilateral nasal polyps. Results of the neurologic examination were normal.

Plain sinus radiographs revealed extensive bony expansion of the right frontal and anterior ethmoid region. A clinical and radiographic diagnosis of a right frontoethmoid mucocele was made. A CT scan was obtained to confirm the diagnosis and assess the extent of the mucocele. Axial and coronal CT revealed marked bony expansion of the right frontal and ethmoid sinuses (see Figure; A,B). The expanded right frontoethmoid complex was compressing the brain posteriorly (see Figure, A). The posterior wall of the mucocele was calcified and thickened. The coronal view shows a mucocele of the supraorbital ethmoid air cells originating in the roof of the right orbit (see Figure, B).

On sagittal reconstruction it was evident that there was bony expansion of the right ethmoid sinuses that extended superiorly and posterior to the expanded frontal sinus (see Figure, C). Sagittal views through the right orbit show bony expansion of the supraorbital ethmoid air cells located in the roof of the orbit (see Figure, D). In the Figure, A, there was a supraorbital ethmoid air cell over the left orbit that was aerated. By CT scan diagnosis, the patient had three mucoceles, involving the right frontal sinus, right ethmoid sinuses, and the supraorbital ethmoid air cells located in the roof of the right orbit.

Bilateral frontal osteoplastic flap, frontal sinus obliteration, and bilateral intranasal ethmoidectomies were performed. Elevation of the flap initially revealed two mucoceles involving the right frontal sinus and the supraorbital ethmoid air cells originating from the roof of the right orbit. Both mucoceles communicated just above the orbit. The posterior wall of both mucoceles was very thin and identified as calcified dura by the consulting neurosurgeon. However, CT scan demonstrated a third, posteriorly located mucocele (see Figure, A), and dissection through the posterior wall of the first two mucoceles (frontal sinus and supraorbital ethmoid mucoceles) revealed a third mucocele involving the ethmoid sinuses. The walls between the three mucoceles were taken down, and the cavity was obliterated with fat. The procedure was completed, and the patient had an uneventful postoperative course.

DISCUSSION

The diagnosis of frontoethmoid mucocele is based primarily on clinical and radiographic findings. Either CT or MRI can be used to demonstrate the conformation and extent of a mucocele in this region. With CT, the majority of mucoceles appear homogeneous and are isodense relative to brain tissue.[2,3] Weber et al[2] analyzed 110 mucoceles and noted calcification in the wall of the mucocele in only five cases (4.5%). Infected mucopyoceles can show rim enhancement with contrast infusion.[3] Computed tomography provides superior bone imaging and can identify bony septa, loculations, and defects. In this case the first mucocele (anterior) represented a right frontal sinus mucocele that was partially connected to a mucocele of the supra-

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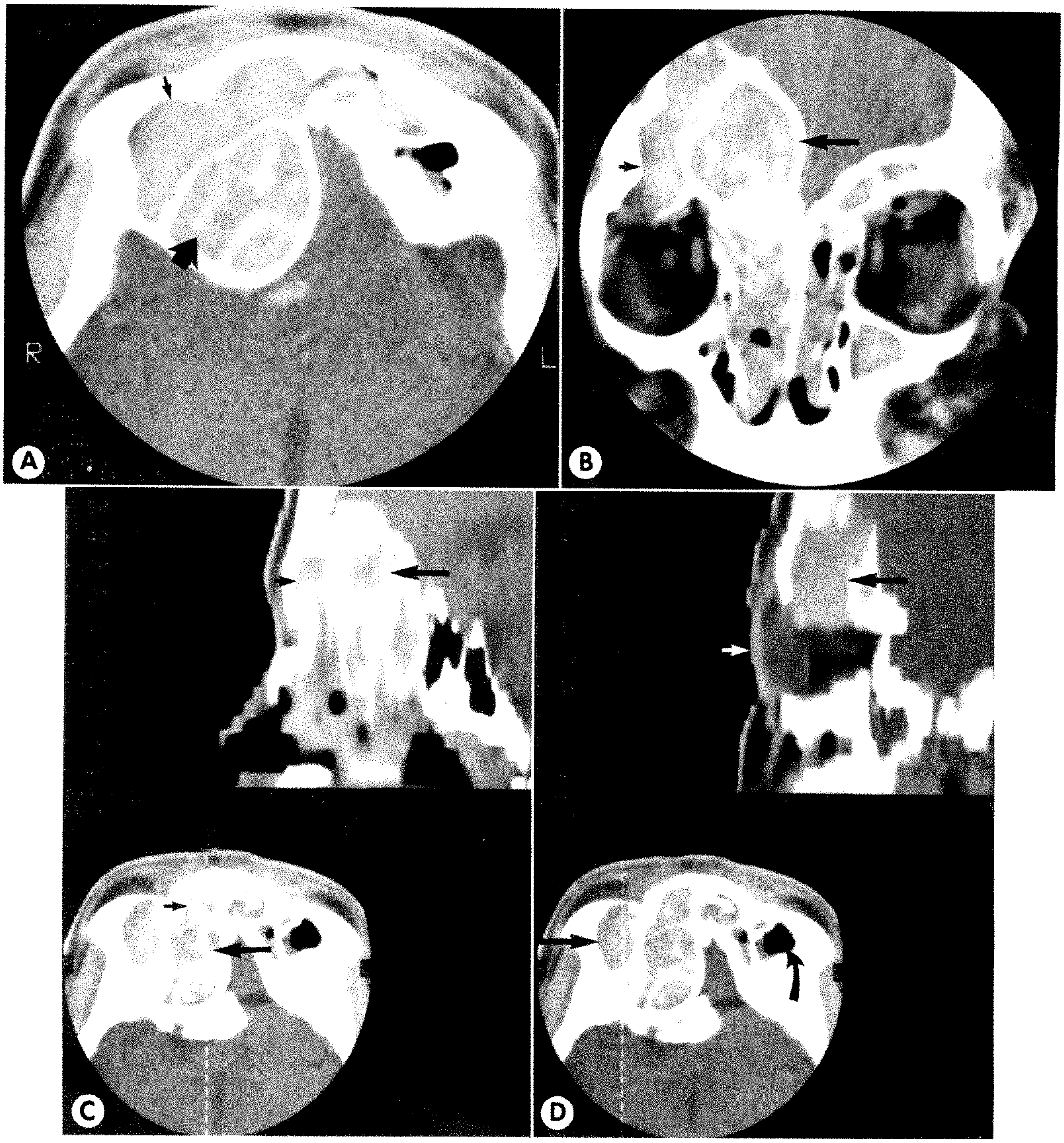

Computed tomographs. A) Axial CT at level of frontal sinus. Note multiple homogeneous frontoethmoid mucoceles. Small arrow — frontal sinus mucocele, large arrow — ethmoid sinus mucocele. B) Coronal CT. Small arrow — mucocele of supraorbital ethmoid air cells originating from right orbital roof, large arrow — ethmoid sinus mucocele. C) Sagittal reconstruction through right ethmoid sinuses. Small arrows — frontal sinus mucocele, large arrows — ethmoid sinus mucocele. D) Sagittal reconstruction through right orbit. Large arrows — supraorbital ethmoid mucocele involving roof of right orbit, small arrow — right globe, curved arrow — aerated supraorbital ethmoid air cells in roof of left orbit.

orbital ethmoid air cells located in the roof of the right orbit. Both of these mucoceles were easily identified after elevation of the osteoplastic flap and were separated by very thin bone from a third mucocele that arose from below in the ethmoid sinuses. Computed tomography was able to accurately image all three mucoceles to provide maximal preoperative information and aid in locating all abnormal mucous collections. The coronal CT views and sagittal reconstruction helped determine the origin of each mucocele and identify the mucocele of the supraorbital ethmoid air cells.

Magnetic resonance imaging provides superior soft tissue contrast and can be used to differentiate a mucocele from a solid tumor of the paranasal sinuses.[3] However, MRI has bone imaging capabilities that are inferior to those of a CT scan. Furthermore, the signal intensity of mucoceles can vary significantly, depending upon their composition and degree of inflammation. Magnetic resonance imaging can aid in the diagnosis of sphenoethmoid mucoceles because of the variety of tumors that can occupy the same area and make diagnosis difficult.[4] This case demonstrates the importance of the bone imaging capability of a CT scan, and we feel it is the superior study for evaluating mucoceles of the paranasal sinuses.

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NIH THERAPEUTIC STUDY OF FOLLICULAR THYROID CARCINOMA

The National Institutes of Health request the cooperation of physicians in referring patients with pure follicular thyroid cancer for a randomized clinical trial that will investigate the effectiveness of radiosensitizing agents in enhancing radioiodine therapy. Patients should have had primary thyroid surgery, without additional therapy for recurrences, and meet one of the following criteria: 1) age 40 years or older at the time of diagnosis with either primary tumor greater than 3 cm, regional lymph node metastases, extensive tumor capsule penetration, or extensive angioinvasion; or 2) any age with either tumor penetration into surrounding tissues or metastases outside of the neck.

All medical care expenses at NIH will be covered by the government except for transportation costs. Physicians will be informed regularly about the status of their patients and will continue to provide long-term care for them. Please write or telephone Dr Kenneth B. Ain or Dr Jacob Robbins, Bldg 10, Rm 8N315, National Institutes of Health, Bethesda, MD 20892; (301) 496-2831 or (301) 496-5761.

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PATHOLOGY CONSULTATION

XANTHOGRANULOMA

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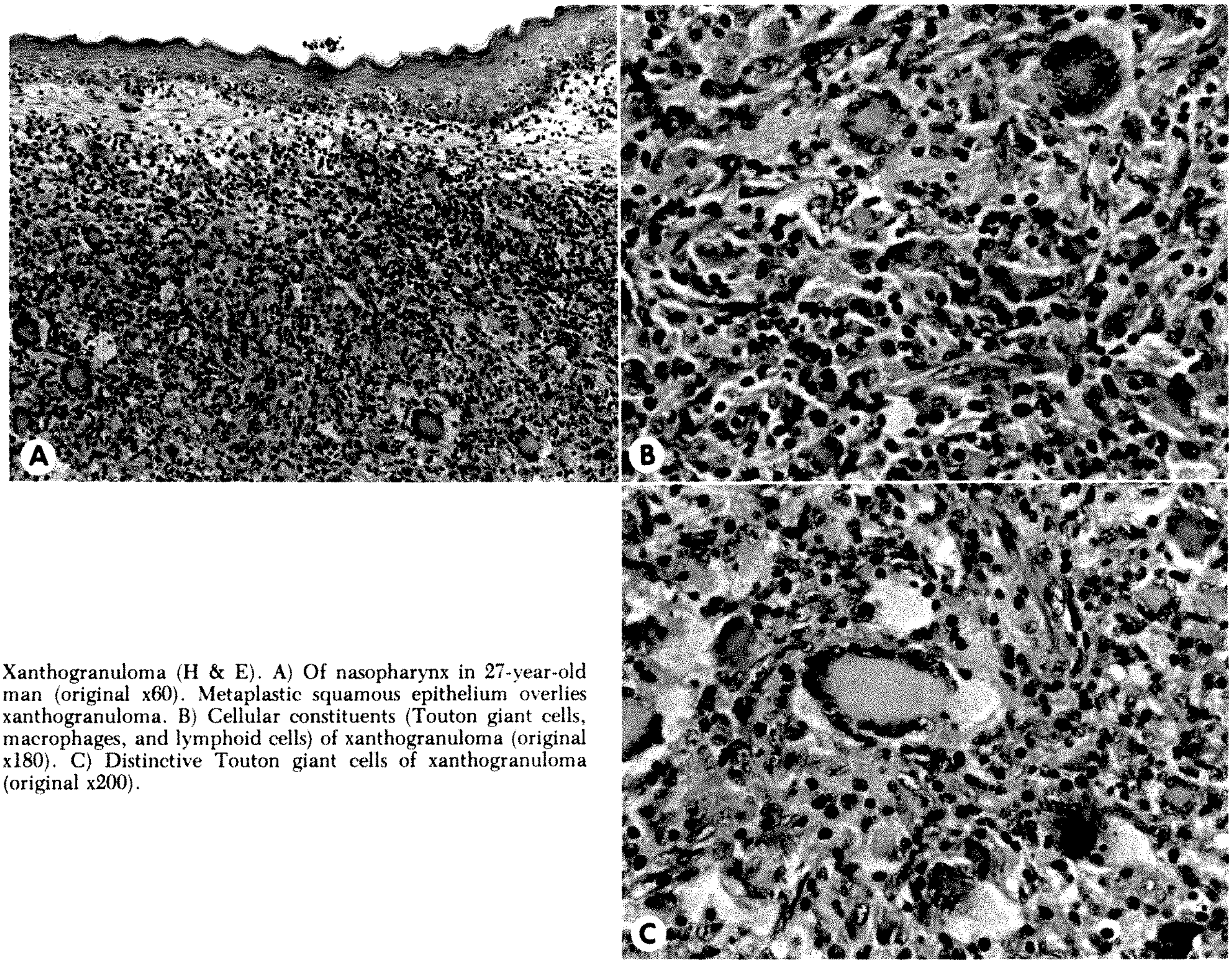
HOUSTON, TEXAS

The skin of the head and neck is an area of predilection for xanthogranuloma, formerly called nevoxanthoendothelioma. Spontaneous resolution is the usual course for this benign, nonneoplastic lesion that is composed of macrophages and Touton giant cells and occurs principally in infants and children. Mucosal lesions occur with or without skin lesions and in the head and neck affect the oral cavity, nasopharynx, and salivary glands.

Considered a nonneoplastic and presumably reactive lesion, xanthogranuloma (nevoxanthoendothelioma) presents in two clinical forms: juvenile and adult.[1,2] The lesions are found preponderantly in infants and young children, in whom they are considered to be the most common xanthoma. The skin of the head and neck is the site of predilection, with most of the lesions making their appearance between the ages of 1 month and 2 years. Approximately 20% are congenital.[1] Both sexes are affected equally, and there is no familial or racial tendency. There is no evidence of an underlying lipid abnormality. Adult forms of xanthogranuloma are histologically indistinguishable from those occurring in



Xanthogranuloma (H & E). A) Of nasopharynx in 27-year-old man (original x60). Metaplastic squamous epithelium overlies xanthogranuloma. B) Cellular constituents (Touton giant cells, macrophages, and lymphoid cells) of xanthogranuloma (original x180). C) Distinctive Touton giant cells of xanthogranuloma (original x200).

From the University of Texas M. D. Anderson Cancer Center, Houston.

REPRINTS — John G. Batsakis, MD, Division of Pathology, University of Texas M. D. Anderson Cancer Center, 1515 Holcombe Blvd, Houston, TX 77030.

the young, but the predilection for involvement of the head and neck is not seen in adults, and spontaneous resolution of the lesions, expected in infant and juvenile patients, is unusual.[1]

Extracutaneous xanthogranulomas, with or without concomitant skin lesions, may be found in either juvenile or adult types. Such occurrences are unusual. Sites of involvement include the oral cavity, nasopharynx (see Figure, A), salivary glands, and soft tissues, including muscle, viscera, and ocular structures. The tongue, palate, gingiva, and tonsillar pillars have been intraoral sites.[1] Eye lesions are the most common extracutaneous manifestations and may involve the iris–ciliary body, epibulbar tissues, and eyelids.[1]

Maculopapular in configuration, xanthogranulomas vary in color from yellow-tan to blue-red, depending on the lipid content and vascularity. Skin lesions may be multiple (25% to 30%) or single and vary in size from a few millimeters to several centimeters in diameter. Mucosal lesions usually are solitary. A susceptibility to bleeding and posttraumatic ulceration is noted at all sites.

Wherever the lesions present, they are characterized microscopically by mixtures of macrophages, giant cells, lymphoid cells, and scant acute inflammatory cells (see Figure, B). Touton giant cells are quite typical of the lesions, although their number is variable (see Figure, C). Macrophages, often lipid-containing, are the preponderant cells, and this is confirmed by ultrastructural examination.[1-3] In the usual cutaneous infantile lesions, the sheets of histiocytic or fibrohistiocytic cells are localized in the dermis with variable extent into deeper subcutaneous tissues. The epidermis and skin appendages are not invaded. Deeply situated lesions are indistinguishable from superficial ones. Most xanthogranulomas display positive immunocytochemical reactions for lysozyme and α1-antichymotrypsin and are negative for S-100 protein antigen.

Xanthogranulomas can be very cellular, and with a diffuse growth and lack of capsule can simulate malignancy, especially in those having deep locations. The macrophage–Touton giant cell combination, age of patients, and locations of involvement are, however, persuasive toward correct diagnosis. These factors, plus few tissue eosinophils and, importantly, an absence of Langerhans granules, exclude a form of histiocytosis X.

Xanthogranulomas characteristically regress over a period of a month to a few years, and except for diagnostic purposes or cosmesis are best left alone if not symptom-producing. Recurrences, more aptly termed persistence, follow too-close or incomplete surgical removal.

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LETTERS TO THE EDITOR

To the Editor:

The American Tinnitus Association is involved in a project to survey physicians in an effort to "tap into" clinical experience they may have accumulated with respect to treatments for idiopathic (garden variety) tinnitus. According to conventional wisdom this condition is very resistant to treatment.

We all know, of course, that many widely used treatments for a wide range of conditions have had their roots originally in clinical experience. However, short of formal research studies, there are few routes for getting clinical hunches out to the medical profession as a whole, much less to the general public.

We realize that in the absence of controlled studies, clinical experience remains in the category of hunches. However, our strategy is to attempt to separate the "signal" (often-reported treatments) from the "noise" (seldom-reported treatments). This strategy may give us some leads that are worth pursuing in more formal research.

If readers have such a hunch concerning a tinnitus treatment that they have not encountered in the medical literature, we'd appreciate their forwarding it to the address below.

Andrew Neher, MA
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PO Box 5
Portland, OR 97207

To the Editor:

Having read with interest Y. P. Krespi and C. J. Meltzer's paper (Laser Surgery for Vocal Cord Carcinoma Involving the Anterior Commissure, *Ann Otol Rhinol Laryngol* 1989;98:105-9), we wish to bring to your attention the following points.

The treatment of T1b and T2 vocal cord carcinoma has long been a subject of controversy. Radiotherapists and many laryngologists usually advocate primary irradiation, whereas other laryngologists recommend partial laryngectomy.[1]

Proponents of radiotherapy contend that survival of patients treated this way does not differ from the survival of those primarily partially laryngectomized.[2] Traditional primary irradiation has been considered to be the optimal management for these cancers, with disease control rates approaching 80%.

However, in our experience tumor volume was a prognostic factor for predicting the outcome of radiotherapy and was of greater significance than age, sex, or T category. Despite the quantitative difference, patients with either small, noninfiltrative glottic tumors or large, invasive T1, T1b, or T2 glottic cancer remain in the same TNM category and have no qualitative oncologic distinction.

The dilemma facing the laryngologist is whether these subgroups belong to the same oncologic category and deserve the same treatment or whether they are different and thus have to be treated differently. We propose to call these subgroups "aggravated" T1, T1b, and T2 tumors (T1Ag, T1bAg, or T2Ag).

In our experience, patients with "aggravated" T1, T1b, and T2 tumors should receive partial or extended vertical laryngectomies as the procedure of choice. This is our policy for treating most horseshoe glottic lesions by frontal or frontolateral laryngectomy.

Reviewing the pertinent literature reveals the following. Kirchner[1] used the term "cold spot" in referring to the failed radiotherapy of the anterior commissure. Olofson et al[2] stated that by using a different radiotherapeutic technique, better results can be obtained. Their crude 5-year survival rate for glottic tumors involving the anterior commissure was 80%, and 70% for true crossing tumors. They noticed that their improved irradiation technique was unsuitable for cancers of the anterior commissure that had any significant subglottic extension because of the clavicular shielding effect. Som and Silver[3] had poor results with primary irradiation, achieving success only in two of 18 patients. Wang and Schultz[4] had a 65% 5-year absolute survival rate in glottic tumors involving the anterior commissure.

Bailey[5] found a local recurrence or a second primary carcinoma of the larynx in 11.4% of 70 consecutive patients followed for longer than 5 years after vertical partial laryngectomy. Perez and Marks,[6] analyzing the results of radiotherapy in glottic carcinoma, report an irradiation control of the primary in 80% of tumors extending to the anterior commissure, but only 77% in patients with involvement of both true vocal cords. Jesse et al[7] claimed an 8.8% failure rate for radiation treatment of 91 T1 and T2 glottic tumors with anterior commissure extension. Lawson and Biller[8] supported the idea that posterior tumoral extension involving the vocal process and anterior face of the arytenoid as well as anterior extension to the commissure changes the biologic behavior of the tumor, decreases cure rate, and diminishes control by radiotherapy. End results, however, were related to the tumor extent. Unilateral lesions with anterior commissure involvement along with less than 10 mm of subglottic extension had a 90% survival rate, dropping to 50% with more than 10 mm of subglottic extension.

Maisel[9] emphasized that the anterior commissure of the larynx is among the most difficult areas of the body in which tumors may be successfully treated by irradiation therapy.

Twenty-two glottic carcinoma patients underwent frontal or extended frontolateral laryngectomy in our department since 1975; all were reconstructed with a composite nasal mucoseptal graft.[10] The 5-year disease-free rate was 95% in that series.

With the existing controversy in the background, it is evident that T staging has its limitations and that more accurate evaluation methods of laryngeal tumor extent are needed. We feel that the tumor heterogeneity exhibited by the "aggravated" form of T1 and T2 tumors should be taken into consideration. Thus, while comparing the results, it is imperative to compare lesions of the same stage as well as the same extent.

We have adopted the following indications for frontal and frontolateral laryngectomy:

1. Recurrence of glottic carcinoma following radiotherapy.
2. Vocal cord carcinoma extending to the arytenoidal vocal process or bulky glottic carcinoma involving more than half of the vocal cord (T1Ag, according to our subclassification).
3. Vocal cord carcinoma infiltrating the ventricular floor (T1Ag).
4. Anterior commissure carcinoma with subglottic extension.
5. Verrucous carcinoma.
6. Supraglottic carcinoma infiltrating the anterior commissure (in which case the anterior commissure procedure will be complementary to the supraglottic laryngectomy).
7. Bilateral vocal cord carcinoma, when more than one third of the length of one or both vocal cords is infiltrated by the tumor (T1Ag).
8. Previous neck irradiation for laryngeal or nonlaryngeal disease.
9. Patients younger than 50 years who are potential candidates for irradiation-induced malignancy.

We support the conclusions of Maisel,[9] Sessions et al,[11] Tucker,[12] and Krespi and Meltzer that for lesions of the anterior commissure, conservation surgery is recommended because of the less satisfactory control rate achieved with radiation therapy.

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BOOK REVIEWS

Keep Your Voice Healthy

Friedrich S. Brodnitz. 2nd ed. Soft cover, illustrated, indexed, 160 pages, 1988. College-Hill Press, San Diego, $19.50.

This volume, which describes the function and care of the human vocal organs, is both instructive and entertaining. Writing in a conversational style, Dr Brodnitz effectively presents valuable information for the person who uses his or her voice as an integral part of daily work. Specifically mentioned are singers, teachers, ministers, actors, salespeople, and so on. This book would be useful as a review for the professional who deals with the human voice and its problems, or as a text to be loaned to patients and clients.

Beginning with a clear, concise description of the anatomy and physiology of the human vocal tract, the author proceeds through the mechanics of voice production, vocal hygiene, and types of disorders and diseases that affect the voice. Included is a chapter that takes the reader on a tour of the laryngologist's examining room and actual examination procedures. The volume ends with a discussion of treatment strategies from the perspectives of all those involved: the patient, physician, speech/language pathologist, and, in some cases, the mental health professional and singing teacher.

Drawing from a wealth of experience as an ear, nose, and throat specialist and expert in the field of voice disorders, Dr Brodnitz gives practical and factual information interspersed with interesting and often humorous anecdotes. Adding to the overall effectiveness of the book are illustrations that help the uninitiated reader comprehend respiration, vocal range, pneumography, and the structure and function of the vocal organs. For the voice professional, this book is a refreshing overview of familiar subjects. For the layperson, this readable text provides practical information regarding the prevention of vocal disorders. At the least, it will direct those who already need special assistance to the appropriate professionals and treatment strategies.

FERNE MCCLINTOCK, MS, CCC-SLP
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The University of Melbourne–Nucleus Multi-Electrode Cochlear Implant

G. M. Clark, P. J. Blamey, A. M. Brown, et al. Volume 38 in *Advances in Oto-Rhino-Laryngology*. C. R. Pfaltz, editor-in-chief. Hard cover, illustrated, indexed, 189 pages, 1987. Karger, New York, $89.50.

The purpose of this monograph is to review the work that led to the development of the University of Melbourne–Nucleus multichannel cochlear implant. This is accomplished by a thorough discussion of the areas involved in this development, namely, physiology, biological safety, engineering, surgery, psychophysics, and speech perception. A section on cochlear implants for prelingually deaf adults and children is also provided.

The major thrust of research undertaken by the authors was to improve speech understanding ability in implant patients, and the major emphasis of the text is on speech perception. This is not surprising in light of the overall aim expressed in the text: "is to develop a cochlear implant that will help profoundly-totally deaf patients understand speech, and also assist them in recognizing environmental sounds."

The development of testing procedures and the test results achieved by actual patients are discussed throughout the book. The conclusions reached by the authors are supported by evidence presented in the text, which is written in a straightforward manner, with rationale given for each step performed. A section describing the surgical procedure with its pitfalls and some helpful suggestions is included, along with appropriate illustrations.

The material is presented in a readable fashion in which the discussions follow a logical developmental order. The text is well documented through the use of numerous tables, graphs, and references.

Even though the scope of this book is dedicated to the University of Melbourne–Nucleus multi-electrode cochlear implant, it would have benefited from a more thorough comparison of the speech processing strategies of other available multichannel implants. Nevertheless, it will be of practical value to those involved in working with the cochlear implant, and should be of interest to otolaryngologists, audiologists, educators of the hearing impaired, and speech pathologists—all potential members of a cochlear implant team. This book would make a significant contribution to the library of any institution or practice in which cochlear implants are performed.

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The Vestibular System: Neurophysiology and Clinical Research

Malcolm D. Graham and John L. Kemink, eds. Hard cover, illustrated, indexed, 669 pages, 1987. Raven Press, New York, $90.

This book represents the work of approximately 80 of the participants in the Barany Society's 13th meeting held in Ann Arbor, Michigan, May 21-24, 1985. The selection of papers presents various aspects of the vestibular system and vestibular testing, but as is typical of such publications, the intricacies of this complex system are not explored fully. The editors are to be commended for coordinating the works of a large number of contributors to a broad menu that includes vestibular research in space, structure and function of end-organs, surgery, metabolic functions, testing, and the vestibulo-ocular response interactions of the cerebellum, CNS, and somatosensory systems. Despite the number and variety of the papers, the editors maintained a format of brevity, clarity, and uniformity in style.

The text is opened with remarks on the personal life of Robert Barany by Professor R. Lorente de No, who collaborated with Dr Barany for many years. This is a fitting introduction, as the thread of Barany's masterful intellect and its imaginative clinical application is woven throughout the chapters.

Today, some 80 years after Barany's most notable contribution to the understanding of the vestibular system and caloric stimulation, scientists still are trying to define the mechanism by which caloric nystagmus is provoked. Only under conditions of microgravity has it been demonstrated that the caloric response can be provoked by means other than those explained by Barany's thermoconvection theory. This is discussed in the book's opening chapter.

Many of the chapters are vivid jewels of specificity. Especially noteworthy is the editors' chapter in which they dissect the results of vestibular nerve sections on their patients with incapacitating vertigo. This report on their 2-year study indicates that non-Meniere patients may well benefit from this surgery, but the outcome is not as predictable as it is in those with classical end-organ disease.

Primarily because this text is an assemblage of papers, it does not give comprehensive coverage of the vestibular system. However, the subject of each section, indeed many chapters, could well serve as the basis of a book. Nevertheless, the editors and authors have provided enough information to stimulate ideas for new laboratory and clinical vestibular research, reevaluation of vestibular testing techniques, application of vestibular studies in other disorders, and modification of vestibular laboratories. It is one of the better texts to come from the "gatherings of a society meeting" and is recommended to all physicians and specialists who are interested in vestibular disorders.

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Pediatric Otology

C. Cremers, G. Hoogland, eds. Volume 40 in *Advances in Oto-Rhino-Laryngology*. C. R. Pfaltz, editor-in-chief. Hard cover, illustrated, indexed, 168 pages, 1988. Karger, New York, $99.50.

This volume is composed of most of the invited papers given at the International Symposium on Pediatric Otology, Nijmegen, the Netherlands, in April 1987. Each of the three main sections of the text is made up of contributions from several authors.

The first section reflects the experience of the authors in the surgical management of congenital aural atresia in children. Of particular interest are the formation of an artificial auricle and treatment of hearing loss in the absence of the oval window with concomitant facial nerve malposition.

A good review of the bacteriology, cytology, biochemistry, and otoimmunology of secretory otitis media is presented in the second section of this text. Also covered are the classifications of the various clinical forms, incidence, risk factors, and causes. In addition, the effects of adenoidectomy, with or without tonsillectomy, is discussed. However, the rationale for not intervening with ventilation tubes before 6 months in the presence of continued effusion is less than convincing.

The major difficulty presented by the third section, which deals with cholesteatoma in children, is that although much has been written about this condition, no significant advancements have been made in its treatment in several years. Therefore, this section deals primarily with a review of the natural history of cholesteatoma, consequences, a functional classification system based on site of origin, and support of staged intact canal wall tympanoplasty as the procedure of choice in both acquired and congenital cholesteatoma in children.

The reader may be disappointed in the lack of "advances" presented in this text. Overall, however, there are some superb surgical maneuvers described for congenital atresia, and Paradise's analysis of research into the cognitive development of children who have had repeated or continuous bouts of secretory otitis media without surgical intervention is revealing and original.

Overall, this text is well done, with adequate literary style. It should serve as a useful source of current information in certain aspects of pediatric otology.

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A Practical Guide to Hearing Aid Usage

Alfred L. Miller. Hard cover, illustrated, indexed, 74 pages, 1988. Charles C Thomas, Springfield, Ill.

Dr Miller accomplishes his purpose of providing for hearing aid users and those who must communicate with them a basic and practical guide. In an easy-to-comprehend fashion, this book adequately discusses adjustments to a hearing aid, but does not go into detailed information regarding the different kinds of aids and their appropriate use. Unfortunately, the author erroneously included the cochlear implant as a hearing aid, thus misrepresenting its intent and function.

The conclusions presented in this text are based on the author's practical experience with hearing aids. However, if manufacturers of hearing aids with specific features are to be discussed, all of those producing aids with specific features should be included. In this respect, Dr Miller's discussion is limited.

The author presents his topic in an organized and easy-to-read manner. The accompanying photographs are a helpful addition to the text. Although most of the information presented should be provided to the patient at the time a hearing aid is dispensed, this text might be useful to the family of a hearing aid user. While it would make no significant contribution to the library of a clinical audiologist, physician, or experienced hearing aid dispenser, this book might be an appropriate and welcome addition to the "waiting room" population.

C. LYNN CARMICHAEL, MSC, CCC-A
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Dermabrasion and Chemical Peel. A Guide for Facial Plastic Surgeons

E. Gaylon McCollough and Phillip Royal Langsdon. Hard cover, illustrated, indexed, 115 pages, 1988. Thieme Medical Publishers, New York.

Drs McCollough and Langsdon have written a monograph that enables the reader to gain significant insight into the techniques of dermabrasion and chemical peel. This superbly written text accomplishes this by providing a detailed discussion of instrumentation, patient selection, surgical techniques, complications, and postoperative care for each technique. The chapters concerning patient selection are invaluable in their detailed discussion of appropriate surgical candidates and the presentation of multiple clear illustrations. In fact, each chapter is clearly written, easy to read, and appropriately illustrated.

Facial plastic surgeons are in a unique position to develop aesthetic surgical practices, and these procedures often will benefit their patients. This book provides an opportunity for residents and inexperienced practitioners to gain a substantial degree of insight into dermabrasion and chemical peeling. In fact, it is an excellent review of these subjects for any skilled surgeon. It should be included in every facial plastic surgeon's library.

JOSEPH B. JACOBS, MD
New York, New York

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Ms. Jane E. Brody, *New York Times*
229 W. 43d Street
New York, N.Y. 10036

July 3, 1989

Dear Ms. Brody:

In your "Personal Health" Column, May 25, 1989, you wrote: "One voice disorder, spastic dysphonia, has no known cause." At least three views exist about the cause of spastic dysphonia: physicians believe the cause is medical; psychiatrists believe it is psychological; and my position as a voice and speech pathologist is that spastic dysphonia is caused by misuse and abuse of the speaking voice. It is a mechanical problem, with psychological overtones. The individual is figuratively talking with the brakes on, squeezing the voice from the lower throat, and the breathing is in the wrong gear.

In 1982, at Cedars-Sinai Medical Hospital, Los Angeles, I presented three patients who had confirmed severe spastic dysphonia to an audience of Ear, Nose, and Throat doctors. These patients told the audience how they had recovered their speaking voices by Direct Voice Rehabilitation. Henry J. Rubin, a well-known ENT specialist, asked after the presentation: "We know that you are the only one successful by speech therapy. Why?" The answer is, I do not do speech therapy. I do Direct Voice Rehabilitation.

Over the past fifteen years, I have been to meetings of the American Speech-Language-Hearing Association, the California Speech-Language-Hearing Association, and the International Association of Logopedics and Phoniatrics, presenting with tapes or with actual patients the recovery from spastic dysphonia by Direct Voice Rehabilitation. In articles and videos (in local TV shows on American Cable and Century Cable) I have reported on 'before' and 'after' patients who have had spastic dysphonia.

The late Henry Fonda had spastic dysphonia. Through a program of Direct Voice Rehabilitation, Mr. Fonda was able to recover his voice and film "On Golden Pond," a movie for which he received an Oscar. Another patient, Dr. Don Dodson said in a *Los Angeles Times* interview that he had fully recovered from spastic dysphonia. Zelda Pollock, who developed spastic dysphonia while teaching, went on KCBS to tell about her recovery.

People come from all over the world for my help in resolving spastic dysphonia. A professor came from the Middle East, having been directed by a medical doctor in the United States, on an RX form, to "chew on a golf ball." By Direct Voice Rehabilitation, the patient recovered in a year. I have received yearly reports from him; he has never lost his voice again. Jim Johnson, a minister from the Mid-West, having had severe spastic dysphonia for almost nine years and trying all kinds of therapy unsuccessfully (even going to the Mayo Clinic), is now talking with a normal voice; he underwent an intensive daily one month program of Direct Voice Rehabilitation with me three years ago. He says his voice recovery is a miracle.

I have found that spastic dysphonia, which I call the monster voice, isn't hopeless and that it has had an excellent prognosis in my office. My techniques differ from those of my colleagues, and I am sharply critical of what some of my colleagues and medical associates do for spastic dysphonia. Patients with spastic dysphonia are usually not given options to surgery and botulism treatment. The downside of these procedures, I find, is not presented to these patients. Direct Voice Rehabilitation is a holistic, conservative, and natural approach to resolving spastic dysphonia, and the patients should be given this as an alternative approach. Are the medical doctors and the speech pathology associations playing the politics of voice?

In 1973 in my textbook, *Modern Techniques of Vocal Rehabilitation,* I wrote about recovery from spastic dysphonia. In my two recent books, *Change Your Voice, Change Your Life* and *Winning With Your Voice,* I discuss the way to get a better, more effective voice, and I detail how those suffering from spastic dysphonia have been helped by my Direct Voice Rehabilitation program.

I am enclosing copies of three of my books as well as a few articles and three thirty minute videos depicting my techniques. I am also including comments of two groups of patients, those who have recovered from spastic dysphonia, and those who are in the process of recovering. I hope you will find this material of interest. I thank you for your kindness in reviewing this response to your article on voice and hope in a future column that you might discuss successful treatment of spastic dysphonia by Direct Voice Rehabilitation.

Most cordially,

Morton Cooper

Morton Cooper, Ph.D.

Let's Hear Your Views!
Please send your comments on spastic dysphonia to MORTON COOPER, Ph.D., Suite 401, 10921 Wilshire Blvd., Los Angeles, CA 90024.

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RESEARCH TRAINING FELLOWSHIPS: For physicians only, fellowship will support 1-2 years' full-time research conducted outside of residency training. Applications must be accompanied by sponsoring institution documentation that facilities and faculty are appropriate for requested research.

DEADLINE: Grant and fellowship applications must be postmarked by **January 31, 1990.**

Information and application materials may be obtained from:

Richard A. Chole, MD, PhD, Secretary-Treasurer
Research Fund of the American Otological Society
University of California, Davis
Otology Lab, 1159 Surge 3
Davis, CA 95616
Telephone: (916) 752-8931

A419

Ceclor®
cefaclor

Summary.
Consult the package literature for prescribing information.

Indications: Otitis media caused by *Streptococcus pneumoniae, Haemophilus influenzae,* staphylococci, and *Streptococcus pyogenes* (group A β-hemolytic streptococci).

Upper respiratory infections, including pharyngitis and tonsillitis, caused by *Streptococcus pyogenes* (group A β-hemolytic streptococci). *Note:* Penicillin is the usual drug of choice in the treatment and prevention of streptococcal infections, including the prophylaxis of rheumatic fever. Ceclor is generally effective in the eradication of streptococci from the nasopharynx; however, substantial data establishing the efficacy of Ceclor in the subsequent prevention of rheumatic fever are not available at present.

Contraindication: Known allergy to cephalosporins.

Warnings: CECLOR SHOULD BE ADMINISTERED CAUTIOUSLY TO PENICILLIN-SENSITIVE PATIENTS. PENICILLINS AND CEPHALOSPORINS SHOW PARTIAL CROSS-ALLERGENICITY. POSSIBLE REACTIONS INCLUDE ANAPHYLAXIS.

Administer cautiously to allergic patients.

Pseudomembranous colitis has been reported with virtually all broad-spectrum antibiotics. It must be considered in differential diagnosis of antibiotic-associated diarrhea. Colon flora is altered by broad-spectrum antibiotic treatment, possibly resulting in antibiotic-associated colitis.

Precautions:

- Discontinue Ceclor in the event of allergic reactions to it.
- Prolonged use may result in overgrowth of nonsusceptible organisms.
- Positive direct Coombs' tests have been reported during treatment with cephalosporins.
- Ceclor should be administered with caution in the presence of markedly impaired renal function. Although dosage adjustments in moderate to severe renal impairment are usually not required, careful clinical observation and laboratory studies should be made.
- Broad-spectrum antibiotics should be prescribed with caution in individuals with a history of gastrointestinal disease, particularly colitis.
- Safety and effectiveness have not been determined in pregnancy, lactation, and infants less than one month old. Ceclor penetrates mother's milk. Exercise caution in prescribing for these patients.

Adverse Reactions: (percentage of patients)

Therapy-related adverse reactions are uncommon. Those reported include:

- Gastrointestinal (mostly diarrhea): 2.5%.
- Symptoms of pseudomembranous colitis may appear either during or after antibiotic treatment.
- Hypersensitivity reactions (including morbilliform eruptions, pruritus, urticaria, and serum-sickness-like reactions that have included erythema multiforme [rarely, Stevens-Johnson syndrome] and toxic epidermal necrolysis or the above skin manifestations accompanied by arthritis/arthralgia, and frequently, fever): 1.5%; usually subside within a few days after cessation of therapy. Serum-sickness-like reactions have been reported more frequently in children than in adults and have usually occurred during or following a second course of therapy with Ceclor. No serious sequelae have been reported. Antihistamines and corticosteroids appear to enhance resolution of the syndrome.
- Cases of anaphylaxis have been reported, half of which have occurred in patients with a history of penicillin allergy.
- As with some penicillins and some other cephalosporins, transient hepatitis and cholestatic jaundice have been reported rarely.
- Rarely, reversible hyperactivity, nervousness, insomnia, confusion, hypertonia, dizziness, and somnolence have been reported.
- Other: eosinophilia, 2%; genital pruritus or vaginitis, less than 1%; and, rarely, thrombocytopenia and reversible interstitial nephritis.

Abnormalities in laboratory results of uncertain etiology

- Slight elevations in hepatic enzymes.
- Transient lymphocytosis, leukopenia, and, rarely, reversible neutropenia.
- Abnormal urinalysis; elevations in BUN or serum creatinine.
- Positive direct Coombs' test.
- False-positive tests for urinary glucose with Benedict's or Fehling's solution and Clinitest® tablets but not with Tes-Tape® (glucose enzymatic test strip, Lilly).

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Additional information available from
Eli Lilly and Company, Indianapolis, Indiana 46285.

Lilly

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Now 1 less dose

New b.i.d. dosing for
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+2 new strengths

187- and 375-mg/5 mL oral suspensions
in 50- and 100-mL-size bottles

Ceclor® cefaclor 187/375

187- and 375-mg/5mL oral suspensions in 50- and 100-mL-size bottles

Experience counts

Penicillin is the usual drug of choice in the treatment of streptococcal infections, including the prophylaxis of rheumatic fever.

Ceclor is contraindicated in patients with known allergy to cephalosporins and should be given cautiously to penicillin-allergic patients.

*Due to susceptible strains of *Streptococcus pneumoniae, Haemophilus influenzae* (ampicillin-susceptible and ampicillin-resistant), staphylococci, and *Streptococcus pyogenes* (group A β-hemolytic streptococci).

†Due to susceptible strains of *S pyogenes* (group A β-hemolytic streptococci).

Lilly

See adjacent page for brief summary of prescribing information.

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